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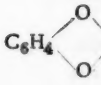
REACTIONS OF TRIARYLBROMOMETHANES WITH (ALKYL)PYROCATECHOL ESTERS OF PHOSPHOROUS ACID

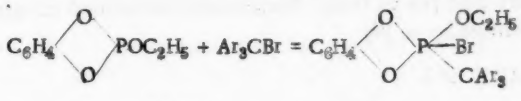
A. E. Arbuzov and F. G. Valitova

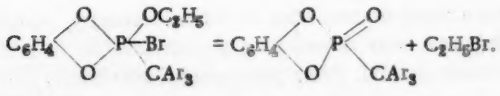
Reactions of the ethyl ester of pyrocatechol phosphorous acid with triarylbromomethanes were studied. The interaction of these compounds gives pyrocatechol triarylmethylphosphinates. On hydrolysis of the latter with dilute hydrochloric acid, pyrocatechol and triarylmethylphosphinic acids are obtained.

The present study deals with the reactions of mixed esters of phosphorous acid, of the type

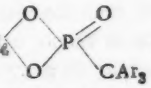

POR (where R is C_2H_5), with triarylbromomethanes.

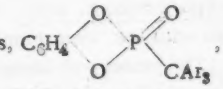
The reaction between (ethyl)pyrocatechol ester of phosphorous acid and triarylbromomethanes should proceed, by analogy with alkyl phosphites, according to the reactions:





It has been shown experimentally that the reaction proceeds indeed according to the equations indicated. Thus, for example, when a mixture of a triarylbromomethane and (ethyl)pyrocatechyl phosphite is heated, evolution of ethyl bromide takes place and a crystalline substance is formed, which is the pyrocatechol ester of triarylmethyl-phosphinic acid. To determine the structure of the obtained compounds the latter were hydrolyzed with dilute hydrochloric acid by heating at 180 to 200° in sealed tubes. The products of hydrolysis were pyrocatechol and triarylmethylphosphinic acids.

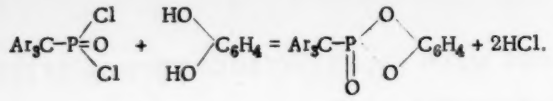
The obtained esters, of the type  , are very stable to atmospheric humidity. Stored in air for a month, they remained completely unaltered; on treatment with water, even when boiled in water, there was no change whatsoever.

Pyrocatechol esters of triarylmethylphosphinic acids,  , are colorless crystalline substances, insoluble in water, alcohol, ether, and difficultly soluble in benzene.

As a result of our research, by reaction of (ethyl)pyrocatechyl phosphite with triphenylbromomethane, diphenyl-biphenylbromomethane, phenyldi(biphenyl)bromomethane, phenylxanthyl bromide, and diphenyl-α-naphthylbromomethane, the respective pyrocatechyl triarylmethylphosphinates were prepared, whereas their hydrolysis gave the corresponding triarylmethylphosphinic acids, except phenylxanthylphosphinic acid. The formulas and melting points of the esters and their product of hydrolysis are given in the table.

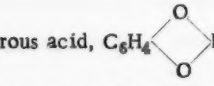
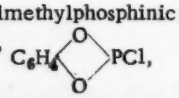
Two esters, with diphenylbiphenylmethyl and phenylbiphenylmethyl radicals, were obtained by A. E. Arbuzov and Nikonorov [1] by another method, in their research on the properties of analogs of the chloride

of Boyd's acid (triarylmethanephosphorylchloride) by reaction of pyrocatechol with triphenylmethyl dichlorophosphine oxide, according to the following equation:

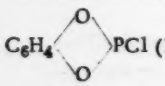


The esters, obtained by us by the method described above, were equivalent in their physicochemical properties to those obtained by Arbuzov and Nikonorov.

Thus, the obtained derivatives of pyrocatechol esters of phosphorous acid and the study of their properties and behavior led to compounds that are similar in structure to compounds prepared from Boyd's acid chlorides, confirming again the viewpoints of A.E. and B. A. Arbuzov [2] on the structure of Boyd's acid chloride as a compound of pentavalent phosphorus.

The (ethyl)pyrocatechol ester of phosphorous acid,  , required for the preparation of pyrocatechol esters of triarylmethylphosphinic acids, was obtained by reaction of absolute alcohol with pyrocatecholphosphinyl chloride,  , according to the method of Milobendzki and Sachanowsky [3], except that pyridine, used to bind the evolving hydrogen chloride, was replaced by dimethylaniline. It should be mentioned that the yield of ester by this method is very high (up to 70%). Pyrocatecholphosphinyl chloride was prepared according to the method of Anschutz as modified by us [4].

EXPERIMENTAL

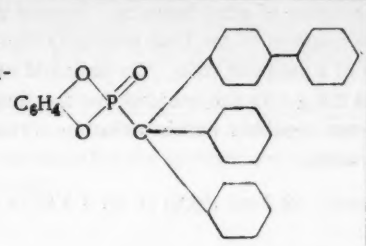
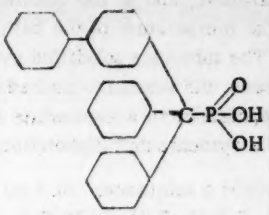
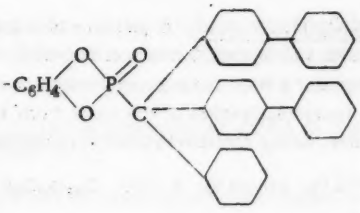
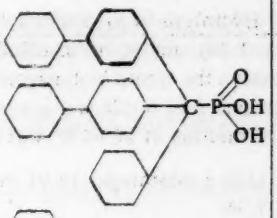
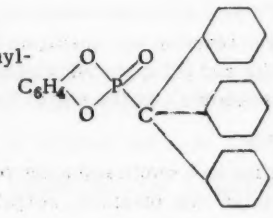
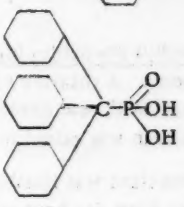
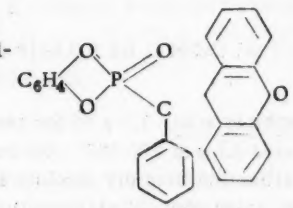
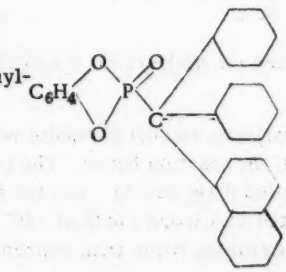
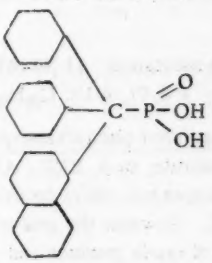
1. Preparation of (ethyl)pyrocatechyl phosphite. Into a round-bottom flask of 750 ml capacity, equipped with a mechanical stirrer, a dropping funnel, and reflux condenser, were placed 84 g dimethylaniline in ether solution and 31.6 g absolute alcohol. With the stirrer in constant motion, 120 g pyrocatecholphosphinyl chloride,  (120 g), dissolved in ether, was added from the dropping funnel. When half of the required quantity had been added, two layers formed in the reactor: a clear bottom layer and a turbid upper layer. Toward the end of the reaction a white precipitate of dimethylaniline hydrochloride separated. When the reaction had come to an end the precipitate was filtered off and washed with dry ether. The filtrate and ether washings were distilled; first the ether was driven off, then the (ethyl)pyrocatechyl phosphite was distilled in vacuo. The ester was purified by threefold redistillation in vacuo, using a three-bulb fractionating column. A fraction boiling at 99-100° at 17 mm was obtained, weighing 88 g. The yield of ester was 69.6%, based on the acid chloride.

2. Pyrocatechyl triphenylmethylphosphinic acid. Into a flask of 50 ml capacity, provided with a discharge tube, extending into the flask, cooled with ice, were placed 7 g (ethyl)pyrocatechyl phosphorous acid and 12.3 g triphenylbromomethane, m.p. 152°. The vessel was heated in a Wood's metal bath. At approximately 100° triphenylmethane began to dissolve gradually and at 150° the reaction began with evolution of vapors, which condensed in the cooled flask. When the reaction was finished, the flask was heated for 2 minutes longer at a bath temperature of 160°. The reaction product was a semitranslucent, viscous, slightly yellow mass, which solidified completely on standing overnight. The obtained substance did not dissolve in alcohol, ether, acetone and was difficultly soluble in benzene. A snow-white powder precipitates as a rule from the benzene solution; however, sometimes regularly shaped crystals separate, most frequently as fine oblong platelets. The yield is almost quantitative. After two-fold recrystallization from dry benzene the substance melts at 186°. The m.p. did not change on subsequent recrystallization. Yield, 10 g.

The obtained substance is pyrocatechyl triphenylmethylphosphinic acid.

0.1165 g substance: 16.8 ml NaOH. 0.1158 g substance: 15.96 ml NaOH. (1 ml NaOH= 0.5618 ml P). Found %: P 8.10, 7.74, $C_{25}H_{19}O_3P$. Calculated %: P 7.78.

The liquid which condensed on the walls of the cooled flask was found to be ethyl bromide. Total evolved, 2.9 g ethyl bromide.

No.	Name and formula	M.p.	Products of hydrolysis	M.p.
1	Pyrocatechyl diphenylbiphenylmethylphosphinic acid 	167-168°	Diphenylbiphenylmethylphosphinic acid 	269-270°
2	Pyrocatechyl phenyldibiphenylmethylphosphinic acid 	194-195	Phenyldi(biphenyl)methylphosphinic acid 	160-162
3	Pyrocatechyl triphenylmethylphosphinic acid 	186	Triphenylmethylphosphinic-acid 	277.5-279
4	Pyrocatechyl phenylxanthylphosphinic acid 	192-193	Not obtained	
5	Pyrocatechyl diphenyl-α-naphthylmethylphosphinic acid 	235-237	Diphenyl-α-naphthylmethylphosphinic acid 	260-263

3. Hydrolysis of pyrocatechyl triphenylmethylphosphinic acid. Pyrocatechyl triphenylmethylphosphinic acid (5 g) was sealed in a tube with 5 ml HCl (sp.gr. 1.13) and 25 ml distilled water. The tube was heated 6 hours at 180°. On cooling, the liquid assumed a light brown coloration, and long needle-shaped crystals and a hard mass, gray in color, separated. The crystals and the mass were filtered off and were recrystallized from absolute alcohol. After five recrystallizations a substance melting at 277.5-279° was obtained as filiform crystals of triphenylmethyl phosphinic acid.

0.1388 g substance: 20.8 ml NaOH. 0.1275 g substance: 19.21 ml NaOH. (1 ml = 0.6239 mg P).
Found %: P 9.34, 9.40. $C_{19}H_{17}O_3P$. Calculated %: P 9.56.

The crystals were sucked off and the filtrate was extracted with ether. On evaporation of the ether, the crystals remaining in the dish were purified by recrystallization from benzene. The obtained substance had the odor of pyrocatechol and melted at 98°, which is close to the m.p. of pyrocatechol (100°).

4. Pyrocatechyl diphenylbiphenylmethylphosphinic acid. A mixture of 2 g (ethyl)pyrocatechyl phosphite and 4.5 g diphenylbiphenylbromomethane, m.p. 125-127°, was heated in a Wood's bath. At 120° the bromide began to dissolve, and at 155° the reaction began with the evolution of ethyl bromide. Toward the end of the reaction the temperature of the bath was raised to 170°. The contents of the flask gradually thickened and discolored. The substance solidified overnight to a glassy mass of a dark-red color. On threefold recrystallization from benzene, the substance melted at 167-168° and weighed 2.5 g. To the unaided eye the obtained substance had the appearance of a snow-white powder; under a microscope regularly formed colorless crystals were seen. The substance is pyrocatechyl diphenylbiphenylmethylphosphinic acid.

0.0996 g substance: 10.3 ml NaOH. 0.1087 g substance: 12.2 ml NaOH (1 ml = 0.6239 mg P). Found %: P 6.45, 7.00. $C_{31}H_{23}O_3P$. Calculated %: P 6.54.

5. Hydrolysis of pyrocatechyl diphenylbiphenylmethylphosphinic acid. A mixture of 2 g of the ester, 5 ml HCl (sp. g. 1.13), and 25 ml distilled water was sealed in a tube and heated 5 hours at 190-200°. On termination of the reaction the liquid had assumed a dark-brown coloration and a hard mass precipitated, covered with a lustrous lacquer (the inside was gray-colored). After fourfold recrystallization of the mass from absolute alcohol, a substance melting at 269-270° was obtained as a white powder, being diphenylbiphenylmethylphosphinic acid.

0.1150 g substance: 14.01 ml NaOH (1 ml = 0.6239 mg P). Found %: P 7.60. $C_{25}H_{21}O_3P$. Calculated %: P 7.75.

6. Pyrocatechyl phenyldi-(biphenyl)methylphosphinic acid. The reaction was analogous to that in the preceding experiments. A mixture of 2 g (ethyl) pyrocatechyl phosphite and 5.1 g phenyldi(biphenyl)methylbromomethane, m.p. 144°, was heated. At 130° the bromide began to dissolve. At the end of the reaction the temperature of the bath was raised to 175°.

When the reaction was finished the contents of the flask solidified to a semitranslucent yellowish mass. Recrystallized twice from dry benzene, a white powder melting at 194-195° was obtained, weighing 1.9 g. The substance is pyrocatechyl phenyldi-(biphenyl)methylphosphinic acid.

0.1243 g substance: 11.5 ml NaOH. 0.1312 g substance: 12.7 ml NaOH (1 ml = 0.5618 mg P). Found %: P 5.19, 5.43. $C_{37}H_{27}O_3P$. Calculated %: P 5.61.

7. Hydrolysis of pyrocatechyl phenyldi-(biphenyl)methylphosphinic acid. 1.3 g of the ester and 5 ml HCl (sp. gr. 1.13), in 25 ml distilled water were sealed in a tube and heated 6 hrs at 190-200°. On termination of the reaction, the separating dark-gray hard mass was purified by recrystallization from dry absolute alcohol. After four recrystallizations, a substance melting at 160-162° was obtained, being phenyldi-(biphenyl)methylphosphinic acid.

0.1127 g substance: 11.70 ml NaOH, 0.1099 g substance: 10.80 ml NaOH (1 ml = 0.6239 mg P). Found %: P 6.47, 6.13. $C_{31}H_{25}O_3P$. Calculated %: P 6.51.

8. Pyrocatechyl phenylxanthylphosphinic acid. To 2.9 g (ethyl)pyrocatechyl phosphite was added 5 g phenylxanthylbromide, m.p. 227°. After 3 to 4 min, without heating, the reaction began. The red color of the bromide disappeared, ethyl bromide evolved, and a white crystalline mass formed. The temperature within the flask was 45°. Towards the end of the reaction the flask was heated in a Wood's bath at 140° for 10 min. This gave 6.2 g of crude product and 1 g ethyl bromide. After recrystallizing twice from benzene, a snow white powder, m.p. 192-193°, was obtained.

Analysis showed that the product is pyrocatechyl phenylxanthylphosphinic acid.

0.1432 g usbstance: 19.9 ml NaOH. 0.2194 g substance: 27.9 ml NaOH (1 ml = 0.5618 mg P). Found %: P 7.80, 7.14. $C_{25}H_{17}O_4P$. Calculated %: P 7.52.

9. Hydrolysis of pyrocatechyl phenylxanthylphosphinic acid with HCl, under conditions analogous to the preceding experiments, did not give the corresponding phenylxanthylphosphinic acid.

10. Pyrocatechyl diphenyl-α-naphthylmethylphosphinic acid. A mixture of 2 g (ethyl)pyrocatechyl phosphite and 3.9 g diphenyl-α-naphthylbromomethane was heated at 170-180°. The reaction proceeded with evolution of ethyl bromide, as before. Toward the end of the reaction the temperature of the bath was raised to 200°. The obtained hard mass gave after twofold recrystallization from benzene a white powder, m.p. 235-237°. Ethyl bromide, 0.8 g.

Analysis gave values corresponding to pyrocatechyl diphenyl-α-naphthylmethylphosphinic acid.

0.1441 g substance: 16.9 ml NaOH. 0.1156 g substance: 13.89 ml NaOH (1 ml = 0.6048 mg P). Found %: P 7.08, 7.26. $C_{29}H_{21}O_3P$. Calculated %: P 6.91.

11. Hydrolysis of pyrocatechyl diphenyl- α-naphthylmethylphosphinic acid. 1.5 g of the ester and 5 ml HCl (sp. gr. 1.13) in 25 ml distilled water was sealed in a tube and heated 5 hours at 200-210°. On termination of the hydrolytic reaction the precipitated mass was recrystallized from absolute alcohol. The obtained crystals melted at 260-263°.

SUMMARY

1. By reaction of (ethyl)pyrocatechyl phosphite with triphenylbromomethane, diphenylbiphenylbromethane, phenyldi-(biphenyl)bromomethane, phenylxanthylbromide, and diphenyl-α-naphthyl bromomethane, the respective pyrocatechol esters of triarylmethylphosphinic acids were obtained.

2. Hydrolysis of pyrocatechol esters of triarylmethylphosphinic acids gives the corresponding triarylmethylphosphinic acids.

3. Pyrocatechyl triarylmethylphosphinic acids, obtained as indicated above, are equivalent in their physicochemical properties to the esters obtained from chlorides of Boyd's acid.

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PHYSICOCHEMICAL ANALYSIS OF SYSTEMS OF MERCURIC HALIDES AND HALIDES OF AMMONIA AND THE ALKALI METALS

I. FUSION OF THE $HgCl_2$–MeCl SYSTEM

I. N. Belyaev and K. E. Mironov

All of the known compounds of $HgHal_2$ and MeHal* were prepared by methods which used water or other solvent solutions of mercury salts [1-4]. Only a few of those reported melted without decomposition; the others as a rule, decomposed into the constituent components on reaching the melting point temperature.

The best known and most stable types of complex compounds of mercuric halides in aqueous media are $Me_2[HgHal_4]$, which often crystallize with several equivalents of water of crystallization [1,2-4]. Compounds of the type $Me[HgHal_3]$ exist with and without water of crystallization. According to Weinland [4], the mercuric salts gave the most abundant series of multinuclear salts with the ratios of $HgHal_2$: MeHal equal to 2:1, 3:2, and 5:1, where the last ratio was for the cations with the largest volumes: ammonium, rubidium, and cesium. The increase in amount of double compounds as a function of the increase in the radius of Me, which were obtained synthetically, can clearly be seen from the reference book [3]. In B. V. Nekrasov's book [5], it is stated that salt types "correspond to the general formulas of $Me[EHal_3]$ to $Me_4[EHal_6]$" and that the tendency of complex formation of mercury and cadmium increases in the order Cl–Br–I.

There was no reference or statement, in the available literature, to any physico-chemical methods of analysis for the study of $HgHal_2$–MeHal systems in the absence of solvents. In the investigations of Beckman [6], on determination of the molecular weights of sodium, potassium, ammonium, rubidium, cesium, and several other metallic chlorides in molten $HgCl_2$, and also that of Guinchant [7] on determination of the potassium, ammonium and other metallic bromides, the amount of MeHal was not greater than 2-7 mole%. The work of Foote and Martin [8], on the electroconductivity of mixtures of $HgCl_2$ and MeCl, when compared by them with the data of Beckman, led to the advancement of certain ideas of the composition of the complex ions in the melts, even though the amount of MeCl did not exceed 3 mole %. Authentic determinations of salts and ions in melts could not be made on the basis of these reports. In view of the above, it appeared to be of considerable interest to study the reaction of mercuric halides with alkali metal and ammonium halides in melts by means of physico-chemical methods.

EXPERIMENTAL

The $HgCl_2$ was the C.P. grade (Karpov), m.p. 280°. The $HgBr_2$ was synthesized from metallic mercury and bromide [9,10]; m.p. 243°. HgI_2 was prepared from mercuric nitrate II by precipitation with potassium iodide, and was purified by sublimation; m.p. 257°. LiCl was prepared from lithium carbonate by the action of HCl followed by drying in a platinum crucible, m.p. 600°. KCl was the C.P. (Khalbaum) preparation. The rest of the reactants were obtained by the recrystallization of C.P. or analytically pure preparations. The salts were carefully dried before use, and were kept in a desiccator over sulfuric acid during the investigation.

Procedure. The systems were studied by the usual visual-polythermic method, given by A. G. Bergman et al [11]. The pyrex test tube used for the substances was placed in a couple of molybdenum glass. A nichrome-constantan thermocouple was used to measure the temperature. It was calibrated by the melting points of chemically pure: naphthalene −80.1°; tin −231.8°; cadmium −320.9°; zinc −419.4°; and a eutectic mixture of 45% KCl and 55% Na_2SO_4 −517.1°. The melting point and the point of disappearance of the crystals were measured on galvanometer with a mirror scale containing 100 graduations. The first crystals in transparent systems were detected with transmitted light. Reflected light and continuous stirring were used with opaque systems (mercuric iodide).

The experiments were complicated by the comparatively small interval between the melting points and the boiling points of the mercuric halides. In order to determine the liquidus curves, the cooling curves of

* Me = the univalent metals Li, Na, K, Rb, Cs, NH_4 . Hal = Cl, Br, I.

certain compositions were partially recorded. During the experiments changes in the substances, visible to the eye, were noted.

TABLE 1

Fusion of the system LiCl–$HgCl_2$

Mole % LiCl	Temp. of appearance of the first crystals	Mole % LiCl	Temp. of appearance of the first crystals
0.0	282.5	1.2	279.5
0.4	282.0	1.8	282.0
0.8	281.0	1.9	297.0

The Chloride Systems. System $HgCl_2$–LiCl. The experiment with lithium chloride was done with every precaution in view of its strong hygroscopicity. According to Table 1, it is apparent that LiCl can dissolve only in small amounts in $HgCl_2$. The melt boiled vigorously when the composition was 1.9 mole % LiCl; $HgCl_2$ distilled but the lithium chloride did not dissolve. The eutectic point occurred at 278° and 1.6 mole % of LiCl. It is interesting that the boiling point of the mixture (297°) was lower than the boiling point of pure $HgCl_2$ (308°).

TABLE 2

Fusion of the system NaCl–$HgCl_2$

No.	Mole % NaCl	Temp. of appearance of the first crystals	No.	Mole % NaCl	Temp. of appearance of the first crystals
1	0.0	283.0	8	16.0	268.5
2	5.0	279.0	9	18.0	276.0
3	10.0	271.5	10	18.9	292.5
4	11.5	270.0	11	20.0	303.0
5	13.0	267.5	12	21.5	309.0
6	14.5	267.5	13	23.0	Melts boiled at 312°; the NaCl did not dissolve.
7	15.2	268.0	–	–	–

NOTES. 1) Eutectic 14 mole % NaCl, 264°. 2) Transition point, 17.5 mole % NaCl, 272°. 3) Transition point, 19.5 mole % NaCl, 298°.

System $HgCl_2$–NaCl. The system was studied up to 23 mole % of NaCl. As the liquidus curve shows (Fig. 1, Table 2), one incongruently melting compound, with a decomposition point at 272°, was formed. The eutectic formed by the chemical compounds and $HgCl_2$ contained 14 mole % of NaCl and melted at 264°.

At 298°, starlike crystals formed which were not observed previously. Apparently, these crystals corresponded to another chemical compound. The composition of this compound can only be determined by a detailed study of the cooling curve. Above 298°, crystals of sodium chloride separated from the melt.

System $HgCl_2$–KCl. The experimental results are given in Fig. 1 and Table 3. The liquidus curve of the system, which was studied up to 65 mole % of KCl (the high melting point of the system prevented further study), contained a series of branches corresponding to the crystallization of the incongruously melting compounds with the composition, $HgCl_2$: KCl equal to: 7:1, 3:2, 1:1 and 1:2. At the higher temperatures, the compound (1:2) decomposed and KCl separated from the melt.

In the region of crystallization of $HgCl_2$, a halt was obtained at 209°, corresponding to the compound $7HgCl_2 \cdot KCl$, which is not shown on the liquidus curve.

System $HgCl_2$–NH_4Cl. This system (Fig. 2, Table 4), the most complete of the systems studied, was studied up to 73 mole % of NH_4Cl. The liquidus curve had a series of transition points corresponding to changes in the solid phase. A chemical compound, composition 1:1, m.p. 218°, and giving a maximum (on the curve) at 50 mole % of NH_4Cl, is shown very clearly on the liquidus curve. Three polymorphic transformations for the compound were found on the cooling curve at temperatures of 213, 207, and 203°. It is interesting to point out that analogous polymorphic transformations were discovered by Wells [12] for the compound $HgCl_2$: CsCl, prepared by a synthetic method in several solvents.

In addition to the 1:1 compound there was still a series of transition points on the liquidus curve at 235, 214, and 243°, corresponding to 23.5, 33.5, and 66.6% NH_4Cl.

According to the given heating and cooling curves, these transition points correspond to the compounds $9HgCl_2 \cdot 2NH_4Cl$, $2HgCl_2 \cdot NH_4Cl$, and $HgCl_2 \cdot 4NH_4Cl$.

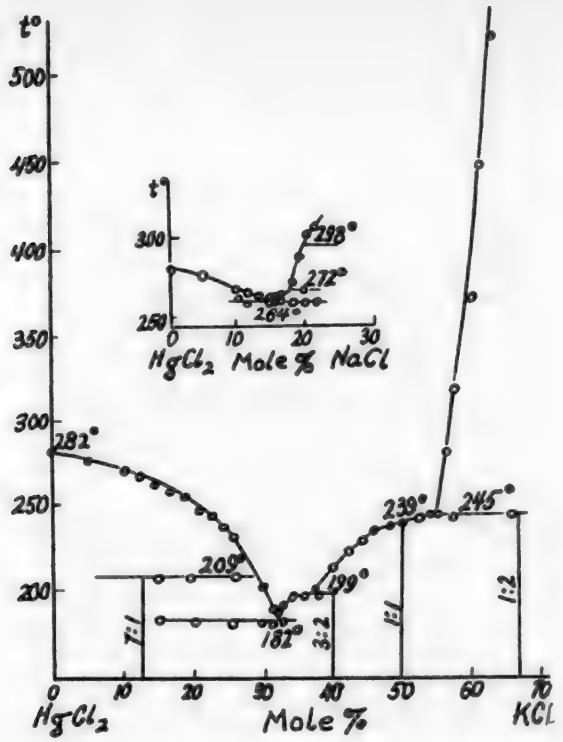

Fig. 1. Fusion of the system $HgCl_2$–NaCl and $HgCl_2$–KCl.

TABLE 4

Fusion of the system NH_4Cl–$HgCl_2$

No.	Mole % NH_4Cl	Temp. of appearance of the first crystals	No.	Mole % NH_4Cl	Temp. of appearance of the first crystals
1	0.0	283.0	18	30.0	228 5
2	2.5	280.0	19	31.5	226.5
3	5.0	275.5	20	32.5	219.5
4	7.5	271.5	21	33.0	214.5
5	10.0	268.0	22	34.0	212.0
6	12.5	263.0	23	35.0	210.0
7	15.0	258.0	24	35.2	209.5
8	16.5	253.0	25	37.0	207.0
9	17.5	249.5	26	37.2	207.0
10	18.0	246.0	27	38.5	205.0
11	19.2	242.0	28	39.0	202.0
12	20.0	240.5	29	40.0	209.5
13	21.0	238.5	30	41.0	209.0
14	22.5	237.0	31	42.0	208.0
15	23.5	235.0	32	42.5	209.5
16	25.0	235.0	33	44.0	212.5
17	27.5	232.0	34	45.0	213.5

(Continued top next page)

TABLE 3

Fusion of the system KCl–$HgCl_2$

No.	Mole % KCl	Temp. of appearance of first crystals
1	0.0	283.0
2	5.0	276.5
3	10.0	271.5
4	12.2	268.0
5	14.5	263.0
6	16.7	259.0
7	18.8	254.5
8	20.7	249.0
9	22.6	244.0
10	24.4	238.0
11	25.6	232.0
12	30.0	203.0
13	31.5	189.0
14	33.0	193.0
15	34.5	197.0
16	36.0	198.0
17	37.5	201.0
18	40.0	213.0
19	42.5	222.0
20	44.0	229.0
21	46.0	234.0
22	48.5	237.0
23	50.0	239.0
24	52.5	242.0
25	54.4	244.0
26	55.0	245.0
27	57.5	318.0
28	60.1	371.0
29	62.5	448.0
30	65.7	523.0

NOTES. 1) Eutectic, 182°, 32 mole % KCl. 2) Transition point, 199°, 37 mole % KCl. 3) Transition point, 239° 50 mole % KCl. 4) Transition point, 245°, 55 mole % KCl. 5) Above 245° and 55 mole %KCl, crystals of potassium chloride separated.

There was no indication of change of phase on the liquidus curve at the concentration between the eutectic at 193° and the transition point at 243°. However, there was a clearly fixed halt on the heating and cooling curves at 210°, corresponding to the compound, $HgCl_2 \cdot 2NH_4Cl$.

TABLE 4(Continued)

No.	Mole % NH_4Cl	Temp. of appearance of the first crystals
35	47.0	214.0
36	48.5	217.5
37	50.0	218.0
38	52.0	215.0
39	54.0	214.0
40	55.0	213.0
41	57.0	210.0
42	59.0	203.0
43	60.0	201.5
44	62.5	209.0
45	63.5	220.0
46	65.0	230.0
47	66.0	237.5
48	66.5	238.5
49	67.0	242.0
50	68.0	251.0
51	69.0	262.0
52	70.0	273.5
53	71.0	296.0
54	73.0	316.0

NOTES. 1) Transition points: 243° and 18.5 mole % NH_4Cl; 235° and 23.5 mole % NH_4Cl; and 214° and 33.5 mole % NH_4Cl. 2) Eutectic points: 198° and 38.7 mole % NH_4Cl, and 193° and 61 mole % NH_4Cl. 3) Maximum at 50 mole % NH_4Cl and 218°. 4) Transition point, 243° and 66.6 mole % NH_4Cl.

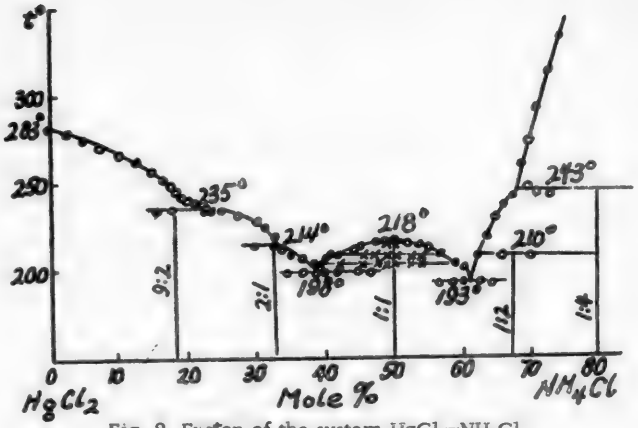

Fig. 2. Fusion of the system $HgCl_2$–NH_4Cl.

Above 243°, NH_4Cl crystallized from the melt. The liquidus curve was stopped at 316° by the distillation of the undissolved NH_4Cl.

TABLE 5

	No. of molecules found in the compound		
	$HgCl_2$	MeCl	H_2O
NH_4Cl [14] .	2	1	1
	1	1	1
	2	3	1
	9	2	–
KCl • . . .	1	1	–
	1	2	1
NaCl•	1	1	–

DISCUSSION OF THE RESULTS

It is apparent from Figs. 1 and 2 and Tables 1-4 that the tendency for complex formation increases with the increase in the radius of the alkali metal cation. For example: in the LiCl–$HgCl_2$ system there was no chemical combination; in the system NaCl–$HgCl_2$, 2 compounds were formed; in the system KCl–$HgCl_2$, 4 compounds were formed; and in the system NH_4Cl–$HgCl_2$, 5 compounds were formed. The most pronounced type of compound was the compound (1:1), whose stability increased with the increase in the radius of the alkali metal cation. In the system NH_4Cl–$HgCl_2$ there is a maximum on the crystallization curve at 218° for this compound.

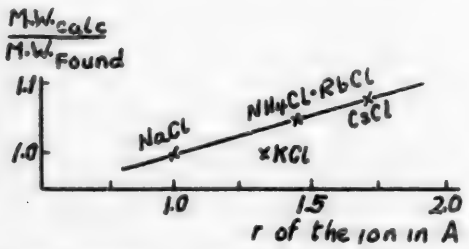

Fig. 3. The ratio $M_{calcd.}/M_{found}$ found as a function of the radius of the cation ($M_{calcd.}$ is the calculated molecular weight, M_{found} is the molecular weight obtained by cryoscopic methods).

The increased complex formation, in the order Li, Na, K, and NH_4 was accompanied by an increase in the angle of incidence on the crystallization curve of mercuric chloride. For cations of large radius, specifically for rubidium and cesium, a large increase in the tendency for complex formation, and a large increase in the angle of incidence of the crystallization curve of $HgCl_2$ must be expected.

The conclusion that complex formation increases with an increase in the radius of the alkali metal agrees well with the results of Beckman [6], if a graph is made of the deviation of the molecular weight found cryoscopically, from that calculated (Fig. 3). From the results

• Systems with NaCl and KCl were studied in the authors' laboratory.

in Fig. 3, it is seen, that this tendency increases in the order Na, K, NH_4, Rb, and Cs.

Lithium chloride behaved analogously to the alkaline earth metals in combination with $HgCl_2$ [8]. This property of lithium had previously been reported by A. G. Bergman.

The study of the ternary water-salts system $HgCl_2$–MeCl–H_2O, where MeCl=NaCl, KCl, and NH_4Cl, showed the same increasing tendency for complex formation. This can be readily seen from Table 5.

SUMMARY

1. The systems: $HgCl_2$–LiCl, $HgCl_2$–NaCl, $HgCl_2$–KCl, and $HgCl_2$–NH_4Cl were studied by the fusion method.

2. An increased tendency for complex formation in the melts, in the order Li → Na → K → NH_4 was found and was found to be accompanied by an increase in the angle of incidence of the same order, on the crystallization curve of $HgCl_2$.

3. The type of fusion diagram for the system $HgCl_2$–LiCl placed it in the same category as the systems "alkali earth chlorides—mercuric chloride".

4. A relation between the molecular weights obtained by cryoscopy and by calculation and the radius of the alkali metal ion, was found in Beckman's results.

5. Three polymorphic transformations in a narrow temperature range (203-213°) were found for the compound (1:1) in the system NH_4Cl–$HgCl_2$.

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PHYSICO-CHEMICAL ANALYSIS OF SYSTEMS OF MERCURIC HALIDES AND HALIDES OF AMMONIA AND THE ALKALI METALS

II. FUSION OF BROMIDE AND IODIDE SYSTEMS

I. N. Belyaev and K. E. Mironov

The results of the fusion studies on chloride systems are given in the previous communication. In this paper, the results of fusion studies on the systems: $HgBr_2$–NaBr, $HgBr_2$–KBr, $HgBr_2$–NH_4Br, HgI_2–NaI, HgI_2–KI, and HgI_2–NH_4I are given.

EXPERIMENTAL

Reactants: $HgBr_2$ — synthesized according to Reinders; HgI_2 — according to Karyakin [1]; sodium, potassium, and ammonium bromides and iodides were twice recrystallized commercial C.P. preparations.

Precedure: All of the iodide systems and that of $HgBr_2$–NaBr were studied by the visual-polythermic method, by reporting the appearance and disappearance of the first crystals, and by visually recording complete heating and cooling curves. For the systems $HgBr_2$–KBr and $HgBr_2$–NH_4Br, the liquidus curve was obtained visually by the appearance of the first and the disappearance of the last crystals. Below the liquidus curve, these sytems were studied by means of heating and cooling curves obtained by a recording potentiometer, IM-148 (the record was made by a plain thermocouple and a recording thermograph) and by recording thermograph (the record was made by a differential thermocouple). These experiments were conducted in closed vessels. The thermocouples, plain and differential, were of nichromeconstatan wire, 0.2 mm in diameter, and were calibrated by the melting points of naphthalene, cadmium, tin, and zinc. All transformations in the system were accurately registered by the plain and differential thermocouples.

I. Bromide Systems

System $HgBr_2$–NaBr. The experimental results are given in Tables 1-3 and Figs. 1-2.

As seen from Fig. 1, the curve, at the beginning of the crystallization, resembled the one reported in the first paper for the chloride system. The system was studied up to 26 mole % of NaBr. The crystallization curve had three main points, one of which was a eutectic point at 232° and 8.5% NaBr*, and two transition points at 243° and 15% NaBr and at 288° and 21% NaBr which corresponded to the compounds of the following probable composition: $HgBr_2 \cdot NaBr$ and $HgBr_2 \cdot 2NaBr$. NaBr crystallized above 288°. The melt boiled at 327° and the NaBr did not dissolve.

System $HgBr_2$–KBr. The system was studied up to 70% KBr. It had five main points; one of which, at 168° and 42.5% KBr, was the eutectic; two at 185° and 190° and 33.3% and 50% KBr were transition eutectic points, and two transition points at 218° and 207° and 17% and 55% KBr.

The transition eutectic-points at 185° and 190° corresponded to: first, the melting point of the eutectic mixture of the compounds $KBr \cdot 2HgBr_2$ and $KBr \cdot 7HgBr_2$, and the melting point of the compound $KBr \cdot 2HgBr_2$; second, the melting point of the eutectic mixture of the compounds $KBr \cdot HgBr_2$ and $2KBr \cdot HgBr_2$ and the melting point of the compound $KBr \cdot HgBr_2$. The transition points at 218° and 207° appeared to be the incongruous melting points corresponding to the compounds $KBr \cdot 7HgBr_2$ and $2KBr \cdot HgBr_2$. The results, therefore, showed that four compounds: $KBr \cdot 7HgBr_2$, melting incongruously at 218° and 17% KBr; $KBr \cdot 2HgBr_2$, melting point 185°; $KBr \cdot HgBr_2$, melting point 190°, and $2KBr \cdot HgBr_2$ melting incongruously at 207° and 55% KBr.

The melts from 35-52% KBr were viscous (glycerine like) and were very prone to supercooling. The experimental results for this part of the liquidus curve were obtained at the disappearance of the last crystals, as well as the appearance of the first; transition temperatures below the liquidus curve were obtained by the heating curve because at this concentration, the transition points were registered at much lower temperatures

* All percentages are molecular.

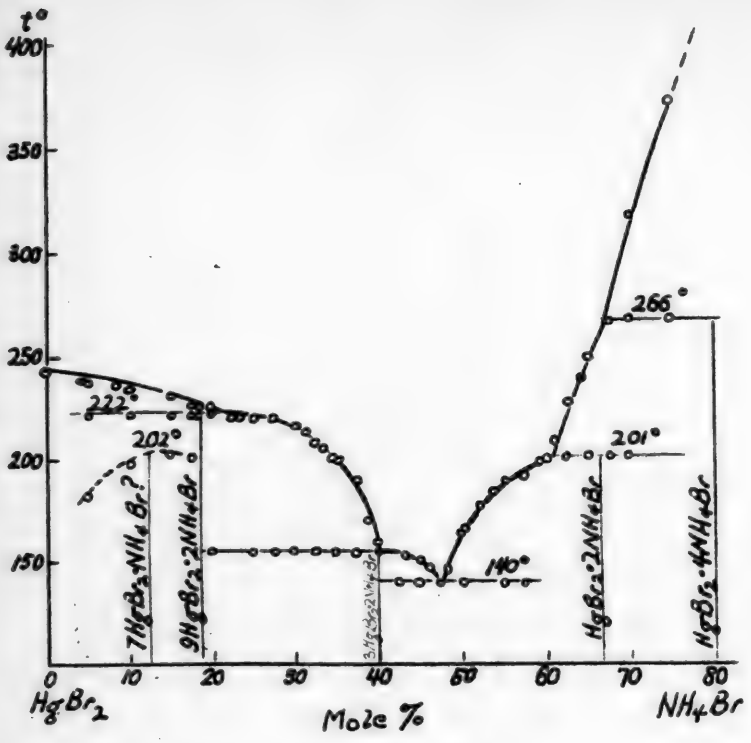

Fig. 2. Fusion of the system $HgBr_2$–NH_4Br

TABLE 4

Fusion of the System HgI_2–NaI

Mole % NaI	Temp. of the appearance of the first crystals	Transition points below the liquidus line	Mole % NaI	Temp. of the appearance of the first crystals	Transition points below the liquidus line
0.0	257.5	127	23.8	226	–
3.9	255.0	–	25.0	220.5	120, 216
4.8	254.0	125	26.6	228.0	–
7.5	253.0	–	28.2	238.5	–
8.3	252.0	120, 217	29.7	253.0	120, 216
10.8	249.0	–	31.2	269.5	–
12.0	248.0	121, 216	33.6	294.0	216, 256
13.9	246.0	–	35.7	317.0	–
15.0	242.0	–	37.7	338.0	–
16.0	241.0	–	39.6	349.0	–
18.2	239.0	120, 216	41.4	367.0	–
20.2	237.0	120, 216	43.0	378.0	–
22.0	232.0	–	44.7	390.0	216, 256
23.2	228.0	–	46.2	At 372°, the melt boils	

System HgI_2–KI. The fusion and the electroconductivity of the system was previously studied by one of the authors. The results of the fusion studies are given in Fig. 3.

System HgI_2–NH_4I. The system was studied up to 75% NH_4I (Fig. 3, Table 5). The presence of two chemical compounds of composition $HgI_2 \cdot 2NH_4I$, and $HgI_2 \cdot 4NH_4I$ was shown on the liquidus curve. On the crystallization curve there was a transformation point at 120°, corresponding to the change of HgI_2 from the yellow to the red modification. The presence of solid solutions of HgI_2 with the compound $2NH_4I \cdot HgI_2$ at 0-7% NH_4I was shown on the cooling curve.

When heated over 210°, violet fumes of iodine vapors filled the test tube; because of this, the liquidus curve after 57% NH_4I was only approximate. At 388° the melt boiled, depositing iodine crystals as it distilled upwards.

Discussion of the results

As seen from the Figures and Tables, the complex formation of the systems $HgBr_2$–MeBr and HgI_2–MeI, as well as that of the systems $MgCl_2$–MeCl, increases with the increase of the volume of the alkali metal cation. The systems $MnCl_2$–MeCl, MgF_2–MeF, and others [3,4] behave analogously.

In the series $HgHal_2$, with the increase of the halogen volume (Cl = 1.81 A, Br = 1.96 A, and I = 2.20 A) the tendency for complex formation decreases, which is shown by the number

TABLE 5

Fusion of the system HgI_2–NH_4I.

Mole % NH_4I	Temp. of appearance of the first crystals	Transition points below the liquidus line
0.0	257.5	127
5.0	254.0	121
7.7	250.0	–
10.0	248.0	120
10.3	248.0	–
12.0	246.0	–
13.2	242.5	–
13.7	242.0	–
14.3	240.0	–
15.0	237.5	–
15.1	238.0	–
15.4	236.0	–
16.6	235.0	–
17.6	232.0	–
18.0	232.5	–
18.7	231.0	–
19.4	230.0	–
19.6	228.5	–
20.7	227.0	120
22.6	219.0	–
24.4	215.0	113.120
25.6	210.0	–
27.5	205.0	–
29.5	197.0	–
31.0	193.0	113,120
33.8	180.0	–
35.0	160.0	113, 120
37.5	145.5	–
38.5	140.0	–
39.4	136.0	–
40.1	132.0	113, 120
40.8	126.0	–
41.5	123.0	–
42.2	122.0	–
42.9	119.0	–
43.1	116.0	–
43.9	126.0	–
44.9	139.0	113
46.2	150.5	–
47.3	160.0	–
48.4	169.0	–
49.5	176.5	–
50.0	182.0	113
50.0	182.0	–
52.3	194.5	–
54.2	201.5	–
56.1	207.0	–
58.0	210.5	–

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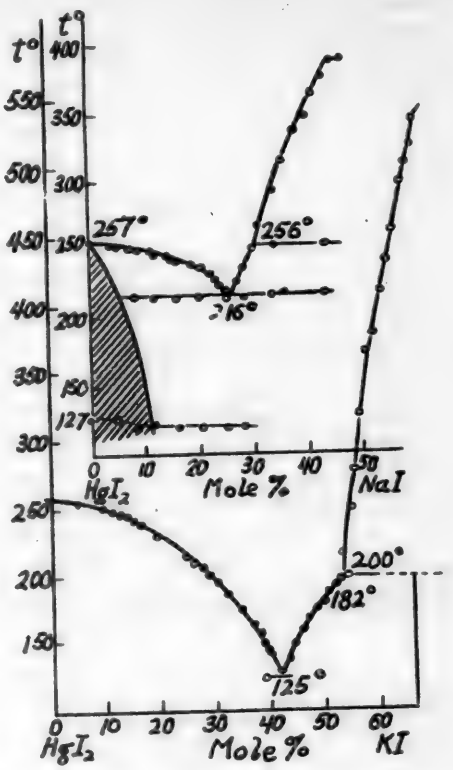

Fig. 3. Fusion of the systems HgI_2–NaI and HgI_2–KI.

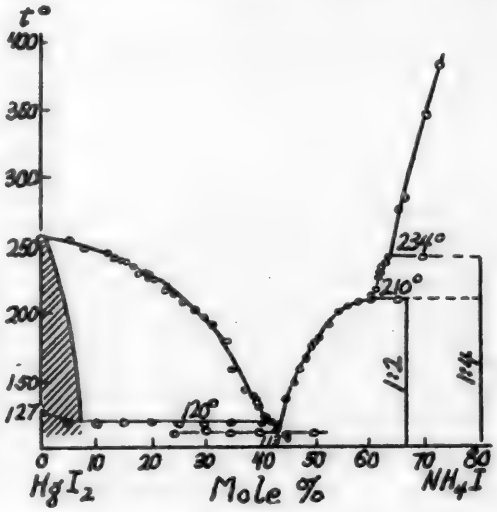

Fig. 4. Fusion of the system HgI_2–NH_4I.

TABLE 5 (Continued)

Mole % NaI	Temp. of appearance of the first crystals	Transition points below the liquidus line
59.6	211.0	–
60.0	211.0	–
60.3	216.0	–
61.0	219.5	–
61.8	227.0	–
62.1	231.5	–
62.5	236.0	–
62.9	239.0	–
63.2	242.5	–
63.3	243.0	–
65.0	278.5	210
66.2	288.0	–
70.1	344.0	234
72.5	385.0	–
74.8	Boils at 388°	

compounds formed. Therefore, in the molten state, in contrast to the aqueous solutions [5], the tendency for complex formation by alkali metal halides with mercuric halides increases in the order I–Cl–Br.

There is a smaller difference in the tendency for complex formation with $HgHal_2$ when the anionic volume is increased along with the cationic radius [6].

When the volume of the halides increases and the cation is unchanged, the eutectic melting point of the melt is lowered (for example: $KCl–HgCl_2$ = 185°, $KBr–HgBr_2$ = 171°, and $KI–HgI_2$ = 125°). With an increase in the volume of the cation in the systems $HgHal_2$–MeHal, a shift of the eutectic melting point of the melt occurs towards that of the MeHal which results in a decrease.

When all of the results are compared, it is seen that the compounds richest in $HgHal_2$ are the chlorides and those rich in MeHal the iodides. The bromides occupy an intermediate position. The most characteristic compounds for all of the halides are $2MeHal \cdot HgHal_2$ and $MeHal \cdot HgHal_2$ (besides $NH_4I \cdot HgI_2$).

For a more descriptive presentation of the relation of the type of compounds to the volumes of the halides and the metal, see Table 6. A summary is given, where the cations, which give the resulting type of compound, are listed under the heading of the halogen.

According to Wells [7], an opposite arrangement must be used for aqueous solutions.

TABLE 6

Type of compound	Cl	Br	I
$7HgHal_2 \cdot MeHal$		NH_4, K	
$4.5HgHal_2 \cdot MeHal$	NH_4	NH_4	
$3HgHal_2 \cdot MeHal$	NH_4	NH_4	
$2HgHal_2 \cdot MeHal$	NH_4	K	
$3HgHal_2 \cdot 2MeHal$	K	NH_4	
$HgHal_2 \cdot MeHal$	NH_4, K, Na	K, Na	K, Na ?
$HgHal_2 \cdot 2MeHal$	NH_4, K, Na	NH_4, K, Na	K, Na
$HgHal_2 \cdot 4MeHal$	K	NH_4	NH_4

SUMMARY

1. The systems $HgBr_2$–NaBr, HgI_2–NaI, HgI_2–KI, and HgI_2–NH_4I were studied by means of the visual-polythermic method. The systems $HgBr_2$–KBr and $HgBr_2$–NH_4Br were studied by means of the visual-polythermic and by thermal methods, with recording of the heating and cooling curves.

2. The tendency for complex formation between the mercuric halides and alkali metal and ammonium halides in melts was shown. Two compounds whose composition was not determined, were formed in the system $HgBr_2$–NaBr; four compounds, $KBr \cdot 7HgBr_2$, $KBr \cdot 2HgBr_2$, $KBr \cdot HgBr_2$, and $2KBr \cdot HgBr_2$ were formed in the system $HgBr_2$–KBr. five compounds, $NH_4Br \cdot 7HgBr_2$, $2NH_4Br \cdot 9HgBr_2$, $2NH_4Br \cdot 3HgBr_2$, $2NH_4Br \cdot HgBr_2$ and $4NH_4Br \cdot HgBr_2$ were found in the system HgBr-NH_4Br; one compound, of clear composition, NaI-HgI_2 was formed in the system $HgI_2 \cdot NaI$. In contrast to aqueous solutions the tendency for complex formation and the stability of the complex increases in the order I – Br – Cl.

3. The most pronounced forms of compounds rich in $HgHal_2$ were the chlorides, and rich in MeHal the iodides. The compound type $Me_2[HgHal_4]$ was present in all systems.

4. The tendency for complex formation increases in the chloride and bromide systems with an increase in the ionic radius of the alkali metal. In iodide systems, the increase in the ionic radius of the alkali metal has little effect on the complex formation.

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KINETICS AND MECHANISM OF THE REACTION OF ACTIVE CHLORINE WITH ORGANIC COMPOUNDS

VIII. OXIDATION OF FORMIC ACID IN ALMOST NEUTRAL AND BASIC SOLUTIONS

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The oxidation of formic acid in acid solutions occurs by means of the action of molecular chlorine on the formate ion [1]. The authors show herein that in basic solutions the oxides of chlorine act as the oxidizing agent, with the hydroxyl ion having an activating effect. At the same time, certain secondary effects become apparent during the oxidation reaction.

Composition of the reaction mixture. As the pH of the solution increases, the form of the active chlorine changes according to the equation $Cl_2 \longrightarrow HOCl \longrightarrow OCl^-$. The amount of each of the components can be calculated from the electrolytic dissociation constant, K_0, of hypochlorous acid and the hydrolysis constant, K, of chlorine. When the concentration of the chloride ion is small, each mixture remains practically two-component because Cl_2 and OCl cannot exist together in commensurate concentrations.

Let h be the concentration of the hydrgen ion, c that of the chloride ion, and C the combined concentration of active chlorine. It is easy to show that for mixtures of HOCl and OCl^- the following expressions hold:

$$[HOCl] = \frac{h \cdot C}{h + K_0} \quad \text{and} \quad [OCl^-] = \frac{K_0 C}{h + K_0} \; ;$$

For mixtures of Cl_2 and HOCl the expressions are:

$$[HOCl] = \frac{K \cdot C}{hc + K} \quad \text{and} \quad [Cl_2] = \frac{hcC}{hc + K} .$$

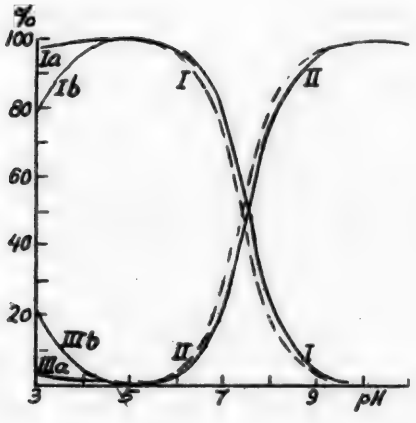


Fig. 1. Composition of chlorine solution vs. the pH.
I) % HOCl; II) % OCl, the solid line is for $K_0 = 3.1 \cdot 10^{-8}$, the broken line for $K_0 = 4.1 \cdot 10^{-8}$; Ia) % HOCl in the presence of 0.01 molar chloride ion; Ib) % HOCl in the presence of 0.1 molar chloride ion; IIIa) % Cl_2 in the presence of 0.01 molar chloride ion; IIIb) % Cl_2 in the presence of 0.1 molar chloride ion.

The given formulas show that when the pH is constant, the concentration of HOCl and OCl^- are proportional to the usual concentration of the active chlorine, C.

The values of the constant K_0 were obtained by several methods (see the summary [2] and [3]) and vary widely. The values obtained by the electrometric titration of hypochlorous acid are the more reliable.

During these studies, the value of the constant K_0 was determined by the titration of the HOCl solutions with a glass electrode in the presence and absence of salt. The value for $K_0 = 3.3 \cdot 10^{-8}$ at 20° was obtained for salt concentrations of about 0.013; here the thermodynamic constant was equal to $3.08 \cdot 10^{-8}$ which is very close to the more reliable values obtained by the same method (average $3.0 \cdot 10^{-8}$). In the presence of 0.5 M KNO_3, the constant K_0 increases to $4.1 \cdot 10^{-8}$.

The value of the hydrolysis constant, K, for the chloride ion is of secondary importance. The result of Yakovkin, equal to $3.78 \cdot 10^{-8}$ at 20° was satisfactory.

The curves in Figure 1 were constructed with aid of the values of K_0 and K which show the changes in percentage composition of solutions of active chlorine at pH's of 3 to 11. The composition curve, calculated for the thermodynamic value of the constant

K_0 ($3.1 \cdot 10^{-8}$) is represented by the solid line, that for the salt, constant K_0 ($4.1 \cdot 10^{-8}$) by the broken line. In acidic solutions, the determination was made at two values of the chloride ion concentration — 0.01 molar and 0.1 molar.

Knowledge of the concentration of chlorine oxide, which forms according to the equilibrium reaction $2HOCl \rightleftarrows Cl_2O + H_2O$, would be valuable for the discussion of the results. According to Goldschmidt [4], at 0°

$$K' = \frac{[Cl_2O]}{[HOCl]^2} = 0.00096.$$

Roth [5] recalculated the results of Goldschmidt and obtained the value K' = 0.00355 (0°). There are no determinations for K' at other temperatures, but Roth found, for 19°, the value K' = 0.0087 by an indirect method. In all cases, in dilute solution, the concentration of Cl_2O is very small when compared to the concentration of hypochlorous acid.

Experimental Method

Preparations. Pure sodium formate was twice recrystallized from water. For comparison, the salt was made from pure formic acid and sodium hydroxide. The salt preparations were dried at 110-120° and carefully tested for the presence of oxalate, carbonate, and chloride impurities. The analytically determined composition of sodium did not differ from the calculated by more than 0.1%.

Hypochlorous acid was obtained by vacuum distillation of solutions obtained by treating chlorine water with silver phosphate. The amount of chlorine in the HOCl solutions was controlled by electrolysis [6].

The buffer solutions were prepared from recrystallized phosphate salts and bases; they were tested in control experiments for their ability to reduce active chlorine.

An electrometric instrument, built according to Sokolov and Pchelin [7], was used to measure the pH in the first series of experiments by means of a glass electrode. In the main series of experiments, an apparatus of the Cambridge system with direct calculation of the pH values was used. The apparatus was standarized with standard solutions of borax and potassium acid phthalate.

The reaction solutions were placed in the thermostat, mainly at 20° ± 0.02°. Several experiments were made at 0°. The flask was covered with metal foil to protect it from light. The test tubes, about 2 ml, were filled by pneumatically regulated pipets, in one series by weight, and in another by volume. The specific gravity of the solution was determined in a parallel experiment in a pycnometer. In view of the relative nonvolatility of hypochlorous acid from solutions, the precautions so necessary for working with chlorine water [1] were not needed.

The amount of active chlorine in the test tube was determined by iodometric titration of small volumes by means of a pneumatic apparatus, observing the usual precautions for this method [8].

The decomposition of hypochlorous acid was controlled in parallel experiments by the addition of buffers. In agreement with Foerster [9], the decomposition of hypochlorous acid in solutions of concentrations up to 0.01 M amounted to less than 1% in 1 hour.

Designation of the symbols. a — the volume of 0.01 N thiosulfate that was used for the titration of 1 ml of the reaction mixture; C — the concentration of active chlorine (in moles per liter); A — the concentration of formate (in moles per liter); Φ — the concentration of phosphate (in moles per liter); the symbol $_0$ means that the given value of the concentration was the initial value of the reaction; t — the time elapsed (in minutes); q' — a third order constant calculated from the constant value of A by the equation:

$$q' = \frac{1}{t} \cdot \frac{1}{AC_0} \cdot \frac{a_0 - a}{a}$$

Experimental Procedure

Concentrations of 0.005-0.01 M for the hypochlorous acid and 0.25-0.5 M for the formate were taken for the kinetic measurements. At higher concentrations, the HOCl tended to decompose in side reactions, and at lower concentrations of formate than those given, the reaction was so slow that the amount of decomposition of the active chlorine increased during the normal course of the reaction.

During the kinetic experiments on the oxidation of formate, an unsatisfactory reproduction of the experimental results was found. Experiments run at various times showed disagreements which could not be accounted

for by the possible experimental error. As an explanation for these results, it was found that the reaction mixture was somewhat sensitive to small amounts of ammonia; this circumstance suggested the known case of the activity of hypochlorous acid for the oxidation of cellulose [10].

Metallic impurities such as copper and ferric salts did not show any catalytic activity.

Because comparatively large amounts of formate and phosphate were used in the experiments, the possibility that small amounts of highly oxidizable impurities were present in them had to be considered.

However, in spite of all of possible measures taken to exclude the possible deterrents (in particular the action of light), the spread of the experimental results was much greater than in other studies on kinetics of reactions with active chlorine. Because of this, when the results of the kinetics of the oxidation of formic acid with active chlorine at a pH of 5 to 10 were examined, certain fixed and sharply defined limits had to be used.

Fig. 2 shows the results of several experiments with identical initial concentrations of reagents: A_0 — 0.25 molar, C_0 — about 0.005 molar. The temperature was 20°. It can be seen that at pH values of 5.5-7, the rate of the reaction depended little on the pH; at higher pH values, the reaction slowed down and finally stopped.

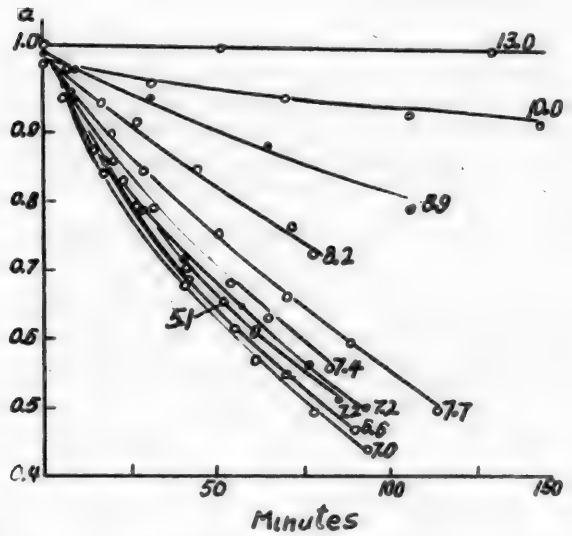


Fig. 2. Decrease of active chlorine titer in reaction mixtures at various pH values (the figures next to the curves correspond to the pH of the solutions).

The conclusions from the kinetic equation

The calculation of the experimental results from each determination, at not too high values of the pH, was obtained at the first stage of the reaction by the secondary kinetic equation for the function of the concentration of the active chlorine:

$$-\frac{dC}{dt} = q'AC^2. \qquad (1)$$

At about half decomposition, the second order constants for the function of C were found to have a tendency to grow. This increase was mainly tied up with the formation of chloride ions. In fact, if potassium chloride is previously introduced into the mixture, the reaction rate increases, more or less, as a function of the concentration of the chloride ion (Fig. 3).

The rate of the reaction is also increased when the new reaction is run in the solution from the old experiment, by the addition of new aliquot of hypochlorous acid to the mixture.

It was very difficult to account accurately for the effect of the chloride ion, and especially on the development of the experiment, when the small losses of hypochlorous acids from decomposition and evaporation become more important. Because of this, examination of the results of the experiments was limited to that part of the experiment in which the concentration of the chloride-ion was still low enough to have no influence on the value of the rate constant. The results of several typical experiments are given below (at 20°). The pH during the course of the reaction was kept with the limits of 0.01-0.02 pH units.

Upon comparing the results of various experiments, it was shown that the constant q' remains stable within experimental limits, with constant pH values, while A_0 changes from 0.05 to 0.5 m and C_0 from 0.0025 to 0.02 m.

With the aid of the constant q', the importance of the reaction by means of elementary chlorine, which is, as is known, the main active agent in acidic solutions [1], can be evaluated. By considering this reaction to be parallel to the reaction by means of hypochlorous acid, it can be shown:

$$-\frac{dC}{dt} = \underset{\text{I}}{q'AC^2} + \underset{\text{II}}{kA[Cl_2]}.$$

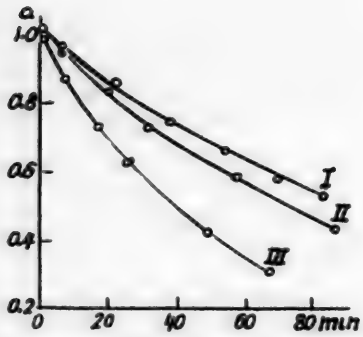


Fig. 3. Velocity of Reaction as a function of chloride concentration
I) without any additions, II) 0.01 molar KCl, III) 0.1 molar KCl. For all experiments: A = 0.25, C = 0.005, Φ = 0.2, pH = 7.55

The value of k in acidic solutions is about 300, the value of q' in the experiments in this study of low pH values approaches 8. Considering that, at low pH values, the main part of the active chlorine is in the form of HOCl, and with the aid of the hydrolysis constant for chlorine, the following ratio of the reaction path II to I for the total reaction path was calculated:

at pH = 5	5.5	6	7	8	9
ratio $\frac{II}{I}$ = 0.2	0.06	0.02	2.10^{-3}	2.10^{-4}	2.10^{-5}

Therefore, at low pH values only, does the reaction by means of Cl_2 have a noticeable effect on the value of the constant q'. Starting at pH 6, this reaction path does not have to be taken into account for calculation of the constant q'.

The above conclusion is based on the premise that the constant k retains its value ($\approx$300) at high pH values. However, results are given below for the use of the hydroxyl ion to increase the rate of the reaction of formate with molecular chlorine. This situation can have a noticeable effect, in cases where a certain amount of chloride ion is present in the solution.

The dependence of the constant q' on the pH is given in Fig. 4, where the deviation of the experimental results from the average is shown.

By evaluating the curve shown in Fig. 4, it is seen that the hypochlorite ion is excluded from the list of direct oxidizing agents for the formate because the oxidation reaction does not occur at all in basic solutions. Because of the appearance of the concentration of the active chlorine, C, in the quadratic form (Equation 1), a concentration for the hypochlorous acid directly proportional to C must be used:

$$[HOCl] = \frac{hC}{h + K_0},$$

where $h = [H^+]$.

The kinetic equation now takes the form:

$$-\frac{dC}{dt} = k'' \frac{h^2}{(h + K_0)^2} AC^2 \quad (2)$$

From equations (1) and (2)

$$k'' = q'\left(\frac{K_0}{h} + 1\right)^2.$$

Table 1 contains the results of the calculations for the values of k'' by means of this formula, using the value of q' obtained from curve in Figure 4. The salt solution value for K_0, $4 \cdot 10^{-8}$, was taken.

Unexpectedly, k'' does not remain constant but increases with increasing pH. It is not difficult to show that the increase of k'' is not related directly to the concentration of either the hydroxyl ion or the hypochlorite ion.

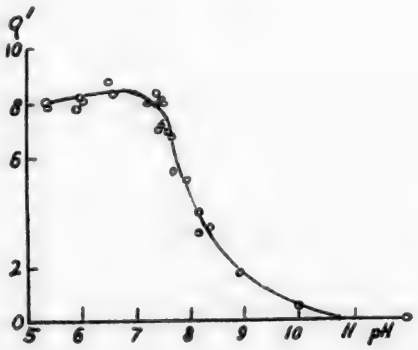


Fig. 4. The variation of the constant q' with the pH.

Experiment 16
pH 5.38, $A_0 = 0.25$
$C_0 = 0.005$, $\Phi = 0.2$

t	a	q'
0	1.015	–
6	0.956	8.1
17.7	0.865	7.7
25.6	0.812	7.7
38.8	0.731	8.0
47.5	0.683	8.0
63.8	0.600	(8.4)
76	0.551	(8.7)
97	0.477	(9.2)
		8.0

Experiment 54
pH 7.16, $A_0 = 0.25$
$C_0 = 0.005$, $\Phi = 0.2$

t	a	q'
0	1.002	–
6.8	0.940	7.8
28.9	0.789	7.44
55.8	0.649	7.8
76.3	0.562	8.2
93.2	0.497	(8.7)
		7.8

Experiment 28
pH 7.5, $A_0 = 0.25$
$C_0 = 0.005$, $\Phi = 0.2$

t	a	q'
0	1.008	–
5.2	0.957	8.0
16.9	0.862	8.0
39	0.718	8.2
62	0.587	(9.1)
70	0.552	(9.3)
120	0.425	(9.0)
		8.1

Experiment 69
pH 7.74, $A_0 = 0.25$
$C_0 = 0.005$, $\Phi = 0.4$

t	a	q'
0	1.013	–
7.2	0.956	6.6
19.5	0.895	5.4
29.8	0.845	5.28
50	0.751	5.4
71	0.661	5.8
88	0.591	(6.4)
114	0.495	(7.3)
		5.6

Experiment 18
pH 8.9, $A_0 = 0.25$
$C_0 = 0.005$, $(KHCO_3) = 0.2$

t	a	q'
0	1.013	–
7.8	0.994	1.9
30.7	0.950	1.7
64	0.880	1.9
105	0.79	2.1
159	0.687	(2.3)
211	0.613	(2.4)
		1.9

Experiment 21
pH 9.95, $A_0 = 0.25$
$C_0 = 0.005$, $(K_2CO_3) = 0.2$

t	a	q'
0	1.008	–
37	0.972	(0.79)
69	0.951	0.68
105	0.929	0.64
144	0.915	0.56
182	0.890	0.58
255	0.853	0.56
309	0.822	0.58
		0.60

However, the results of the experiments may be expressed by means of two kinetic equations, one of which is proportional to the concentration of the OH^-.

$$-\frac{dC}{dt} = k_2 A[HOCl]^2 + k_2 A[HOCl]^2[OH^-] \quad (3)$$

or

$$-\frac{dC}{dt} = (k_2 + k_2' [OH^-])A[HOCl]^2.$$

Evidently,

$$k_2 + k_2' [OH^-] = q'\left(\frac{K_0}{h} + 1\right)^2 = k''. \quad (4)$$

The value of k_2 can be obtained, by considering that at pH 5-6, the value of $k'[OH^-]$ is still very small in comparison to that of k_2: $k_2 = 8$ was used. The values of $k_2'[OH^-]$ and k_2' were found from Formula (4) by using this figure (Table 1).

TABLE 1

pH	q'	$\frac{K_0}{h} + 1$	$\left(\frac{K_0}{h} + 1\right)^2$	k''	$k_2'[OH^-]$	$10^{-8} k_2'$
5.5	8	1.013	1.04	8.3	0.3	0.95
6	8.2	1.04	1.08	8.9	0.9	0.90
7	8.4	1.4	1.96	16.5	8.5	0.85
8	5	5	25	125	117	1.17
9	1.6	41	1681	$2.7 \cdot 10^3$	$2.7 \cdot 10^3$	2.7
10	0.4	401	$1.6 \cdot 10^5$	$6.1 \cdot 10^4$	$6.4 \cdot 10^4$	(6.4)
						$k_2' \approx 1.10^8$

The conditions for the determination of k_2' are generally not very favorable for accuracy. At low pH values, k_2 must be calculated from the difference between $k'' - k_2$. At high pH values the value of k_2' becomes very inaccurate because it is necessary to multiply q' by the coefficient $\left(1 + \frac{K_0}{h}\right)^2$, which contains a large amount of errors in the values of K_0 and h.

A study of these results shows that the permanency of the constant k_2' at least in the order of its magnitude, confirms the presence of a kinetic term proportional to the concentration of the OH^-.

Effect of the buffers added. The salts of the weak acids in concentrations of 0.1-0.4 showed a small, and in most cases, a moderating effect upon the reaction. Phosphates were less active than borates and phthalates, and in basic media, could, apparently increase the reaction rate slightly. The data for this summary is found in Table 2, where the results of several experiments, under the best possible parallel conditions, are given. For non-buffered solutions where the pH gradually increased, the constants and the pH for zero decomposition were used.

TABLE 2

Experiment	pH	Buffer	Molar concentration of buffer salt	q'
19	5.39	–	–	8.8
17	5.4	Phthalate	0.1	6
16	5.38	Phosphate	0.2	8
31	7.4	–	–	6
32	7.4	Nitrate	0.2	6.8
38	7.4	Phosphate	0.2	7.8
30	7.4	Phosphate	0.4	8
47	8.2	–	–	2.0
45	8.2	Borate	0.2	1.1
46	8.2	Phosphate	0.2	3.2

Temperature coefficient for the reaction rate. Several kinetic experiments on the oxidation of formate at 0°, without the addition of buffers, were made. These experiments showed that a decrease in the temperature of 20° caused an almost ten-fold decrease in the reaction rate. Calculation of the constants $\underline{q'}$ and $\underline{k_2'}$ was difficult because the glass electrode could not be used to measure the pH at 0° and an accurate value of the electrolytic dissociation constant for hypochlorous acid for 0° was not known.

Mechanism of the Oxidation of the Formate ion.

The quadratic form, in which the concentration of HOCl is found in the Kinetic Equation (3), shows that the active oxidizing agent for the oxidation of formate appears to be chlorine oxide, which is related to the concentration of HOCl by the equilibrium equation:

$$2HOCl \rightleftharpoons Cl_2O + H_2O.$$

As is known, certain addition reactions of HOCl proceed by means of chlorine oxide, wherein the Cl_2O formation rate can limit the overall reaction rate [11]. The consecutiveness of these reactions is due to the fact that the concentration of the organic compound enters into the kinetic equation in a lower order. In these cases an increase in the hydroxyl ion concentration, which increases the rate of chlorine oxide formation, increases the reaction and removes, or lessens, the consecutive effect. The reactions studied go so slowly that the reaction for the formation of the chlorine oxide cannot limit the overall oxidation rate. Because of this, the equilibrium concentration of chlorine oxide is always assured in the experiments on the oxidation of formate. In agreement with this, no signs of consecutiveness were noticed upon increasing the formate concentration. Therefore, some other explanation for the catalytic action of the hydroxyl ion must be sought.

The form of the second term of the Kinetic Equation (3) leads to two possibilities: the OH^- acts, either on the hypochlorous acid, or on the formate ion. These possibilities are kinetically inseparable. In the first case, the product of $[HOCl]^2\,[OH^-]$ can be changed to the proportional quantity [HOCl] [OCl], and in this way one returns to Kaufman's hypothesis postulating the existence of the complex $HOCl \cdot OCl^-$ [12], which is disclaimed by the author at the present time [10]. Kinetic considerations in other reactions of hypochlorous acid give no evidence for the existence of the Kaufman type complex compounds.

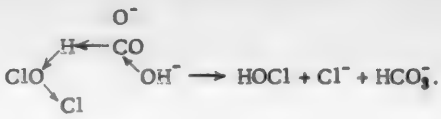
On the other hand, the action of the hydroxyl ion on the formate would indicate that the formate ion forms a salt of orthoformic acid with the hydroxyl ion:

$$HCO_2^- + OH^- \rightleftharpoons \left[\begin{matrix} OH \\ HCO \\ O \end{matrix}\right]^{--}.$$

If such a reaction were allowed, the form of the Kinetic Equation (3) would be explained. However, it is difficult, apparently, to assign such a degree of acidity to the formate ion, which is necessary in order to lead to the formation of a sufficient amount of orthoformate salts to account for the observed reaction rates. Because of this, it is proposed that the hydroxyl ion acts, at the time of the reaction, on the complex which forms initially between the chlorine oxide and the formate ion according to the following outline:

$$Cl_2O + HCO_2^- \rightarrow \begin{matrix} O \\ CO^- \\ H \\ ClO \\ Cl \end{matrix} \qquad (I)$$

The complex (I) supposedly can split into stable compounds without the aid of the hydroxyl ion, by eliminating CO_2 by the action of a molecule of water. However, decomposition of the complex proceeds more readily if the OH^- enters into the reaction:



Therefore, the increase in the reaction rate is due to the nucleophyllic effect of the hydroxyl ion.

An analogous proposal can be made to explain the catalytic action of the chloride, which was shown experimentally above. As was shown during the discussion of the amount of the reaction going by means of elementary chlorine, the reaction by means of Cl_2 becomes insignificant as compared to the reaction by means of HOCl even at pH values of 6-7. However, this conclusion was made on the basis of the comparison of reaction rates in acidic media when the action of OH^- is absent. If it is considered that the hydroxyl ion can ease the decomposition of the complex between chlorine and the formate ion, then the action of the chloride ion must also be more effective at higher pH values. This is, possibly, related to the increase of the reaction rate on the increase of the concentration of the chloride ion in the reaction mixture.

SUMMARY

1. The kinetics of the oxidation of formic acid at pH values of 5 to 10 with small concentrations of the chloride ion can be expressed by the general kinetic equation:

$$-\frac{dC}{dt} = k[HCO_2^-][Cl_2] + k_2[HCO_2^-][HOCl]^2 + k_2'[HCO_2^-][HOCl]^2[OH^-].$$

At 20° $k_2 = 8$, $k_2' \sim 1 \cdot 10^8$; k on the basis of previous measurements [1] is equal to ~ 300; in agreement with which, the first term in the kinetic equation has a definite value only when the pH is at the lowest value in the range studied.

2. The chlorine ion increases the reaction rate somewhat, which leads to the increase of the third order constant during the development of the reaction.

3. Salts of weak acids have a small moderating or stimulating effect on the oxidation reaction of formic acid.

4. At 0° the oxidation reaction of the formate is about 10 times slower than at 20°.

5. The main oxidizing agent for the formate in the pH range studied appears to be chlorine oxide. The catalytic action of the hydroxyl, expressed in the last term of the kinetic equation, is explained by the nucleophyllic effect of the hydroxyl ion, which aids the decomposition of the initially formed complex between HCO_2^- and chlorine oxide.

The analogous catalytic effect of the chloride ion is combined with the nucleophyllic effect of the hydroxyl ion in the reaction between formate and molecular chlorine.

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KINETICS OF THE OXIDATION OF POLYISOBUTYLENE

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In a series of reports [1,2] it was shown that the thermal initiation of oxidative processes for unsaturated rubbers depended upon the reaction of oxygen with double bonds located throughout the main chains of the molecule. It was also determined that the development of real conditions for the oxidation of rubber was limited by the initiation acts. In connection with this, it seemed very interesting to study the initiation mechanism for saturated polymers which lack double bonds. As models for experimentation, polyiosbutylene and butyl rubber were chosen.

EXPERIMENTAL

For purification, polyiosbutylene was dissolved in chloroform, filtered through a glass filter, and precipitated from a 2.5% solution with methanol (the chloroform and methanol were initially purified). After two reprecipitations, the polyisobutylene was dried to constant weight in vacuum. All the operations for the purification of polyisobutylene were conducted in the atmosphere.

The butyl rubber was reprecipitated from benzene. The operations for its purifications were made in nitrogen.

The study of the inhibition and free development of the autocatalytic oxidation of polymers was conducted by means of methods given by one of the authors [3,4].

The oxidation of polyisobutylene was conducted in flat-bottomed glass dishes, 30 mm in diameter and 3 mm high; 15 of such dishes, with films of polyisobutylene, were placed on a glass shelf in the reaction vessel.

In order to characterize structural changes in the polymers which occurred during the oxidation, the viscosity of solutions of the polymers was determined at various stages of the reaction. The viscosity was measured with an Ostwald viscosimeter (capillary diameter 0.3 mm) at 25°. The solutions which were used for viscosity measurements had a concentration of 0.3%.

1. Oxidation of Polyisobutylene

Fig. 1 and Table 1 contain the results of the study of the inhibited* oxidation of polyisobutylene at 110°.

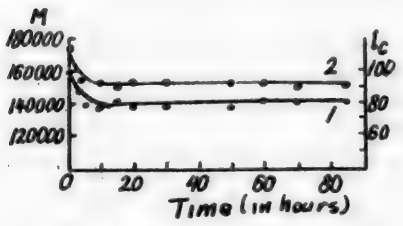


Fig. 1. The Kinetics of the consumption of the inhibitor and the decrease of the molecular weight of polyisobutylene during the process of oxidation at 110°. 1) Consumption of the inhibitor; 2) Change of the molecular weight; i_c - the free inhibitor (in %); M - the molecular weight.

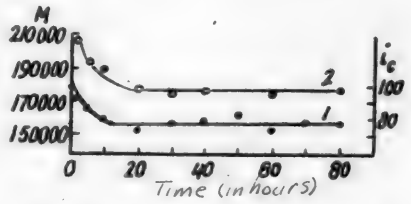


Fig. 2. The Kinetics of the consumption of the inhibitor and the decrease of the molecular weight of polyisobutylene during the process of oxidation at 130°. 1) Consumption of the inhibitor; 2) Change of the molecular weight; i_c - the free inhibitor (in %); M - the molecular weight.

As can be seen in Fig. 1 the inhibitor was only consumed during the first 5 hours of oxidation; thereafter the concentration of the inhibitor did not change. The greatest consumption of the inhibitor did not exceed 20% of

* In the rest of the text "inhibited oxidation" will mean oxidation in the presence of phenyl-β-naphthylamine (inhibitor).

its initial concentration. The molecular weight, also, decreased only 14% at the beginning of the experiment, and later on did not change at all. The consumption of the inhibitor and the decrease of the molecular weight occured simultaneously.

Fig. 2 and Table 2 contain the results of the consumption of the inhibitor and the decrease of the molecular weight for oxidation at 130°.

TABLE 1

Consumption of the inhibitor and change in the molecular weight of polyisobutylene during the oxidation at 110°.

Initial concentration of the inhibitor was 1.28 millimoles/liter (0.5%)

Oxidation time (in hours)	Inhibitor		Molecular weight $M.w.\cdot10^{-3}$
	Free (%)	Consumed (%)	
0	100.0	0	175.0
2.5	87.0	–	–
5	75.0	21.4	152.7
10	74.0	24.1	152.0
15	75.0	21.7	148.0
20	72.0	22.2	152.0
30	74.0	20.2	151.6
50	72.0	18.1	151.0
60	75.0	12.7	151.0
70	76.0	12.4	146.3
80	75.0	19.4	148.8

TABLE 2

Consumption of the inhibitor and change in the molecular weight of polyisobutylene during the oxidation at 130°.

Initial concentration of the inhibot was 1.28 millimoles/liter (0.5%)

Oxidation time (in hours)	Inhibitor		Molecular weight $M.w.\cdot10^{-3}$
	Free (%)	Consumed (%)	
0	100	0	194.0
2	90.3	10.3	207.0
5	87.2	19.6	194.0
10	79.5	25.6	180.0
20	73.0	34.1	178.0
30	93.1	21.0	174.0
40	81.5	–	177.0
50	85.5	10.5	–
60	79.1	19.3	176.0
70	82.1	23.2	160.0
80	82.8	16.4	177.0

Here, as at 110°, the consumption of the inhibitor and the decrease in the molecular weight occured simultaneously at the beginning of the experiment. The inhibitor was consumed to an extent of 25% of the initial amount.

The above changes were recorded during 20-25 hours.

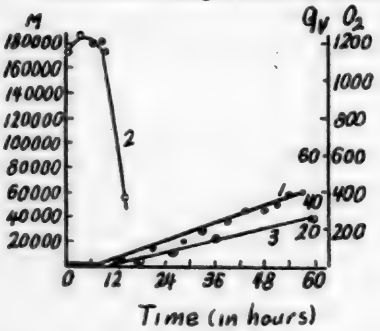


Fig. 3. Autocatalytic oxidation of polyisobutylene at 110°.
1) Addition of oxygen; 2) decrease in molecular weight; 3) separation of volatile products from the reaction; M - molecular weight; Q_V - amount of volatile reaction products (in %); O_2 - amount of added oxygen (in millimole/mole).

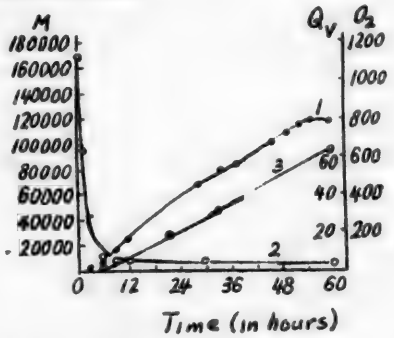


Fig. 4. Autocatalytic oxidation of polyisobutylene at 120°.
1) Addition of oxygen; 2) decrease in molecular weight; 3) separation of volatile products from the reaction; M - molecular weight; Q_V - amount of volatile reaction products (in %); O_2 - amount of added oxygen (in millimole/mole).

The free development of the autocatalytic process for polyisobutylene at all temperatures is characterized by a considerable decrease in molecular weight and the separation of a large amount of volatile products.

Fig. 3 contains the curves for the addition of oxygen, the separation of volatile products, and the decrease in the molecular weight of polyisobutylene for oxidation at 110°.

As it is seen from Figure 3 the rate of decrease in the molecular weight is proportional to the rate of oxidation. In the first stages of the reaction, a small increase in the molecular weight occurred which, however, lies within the limits of experimental error. The separation of measurable amounts of volatile products only started when the molecular weight fell to 80,000. Apparently the deep rooted decomposition did not occur in the initial polymer but in the products of its early destruction.

Figure 4 contains the curves which illustrate the oxidation of polyisobutylene at 120°. Here, the decrease in the molecular weight is more pronounced than at 110°. The molecular weight decreased 95% (from 175,000 to 10,000) in the early stages of the reaction. Again, separation of the volatile products began only after the initial fall in the molecular weight.

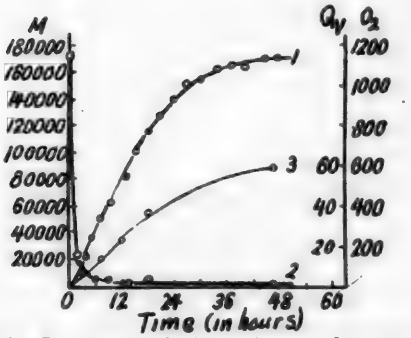


Fig. 5. Autocatalytic oxidation of polyisobutylene at 130°. 1) Addition of oxygen; 2) decrease in the the molecular weight; 3) separation of volatile products; M - molecular weight; Q_V - amount of volatile products of the reaction (in %); O_2 - amount of added oxygen (in millimoles/mole.).

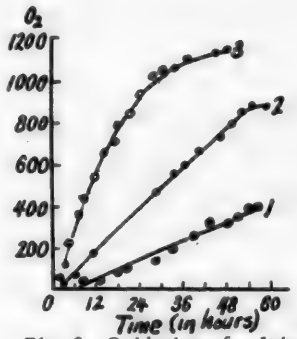


Fig. 6. Oxidation of polyisobutylene at various temperatures. 1) 110°; 2) 120°; 3) 130°; O_2 - amount of oxygen added (in millimoles/mole.).

Only a small portion (about 50 millimoles/mole) of the usual amount of oxygen, which takes part in the oxidation of the polymer, was used for the initial destruction of the molecular chain. The main part of the oxygen was used for the extensive oxidation of the fragments. This is evident from the amount of volatile products formed, which amounted to 60% of the usual weight of the polymer, and the oxygen added.

Fig. 5 contains the curves which are characteristic for the oxidation of polyisobutylene at 130°. Here, the general picture of the oxidation resembles that of the corresponding reaction at 120°. Of course, the addition of oxygen and the oxidative destruction occurred more intensively here.

Fig. 6 contains the kinetic curves for the oxidation of polyisobutylene at various temperatures. Table 3 contains the corresponding numerical data.

The change of the temperature has a great effect on the rate of oxidation of polyisobutylene. The temperature coefficient, corresponding to the stationary reaction rate, lies within the limits of 2-3. The maximum amount of oxygen used increases with the temperatures. If the maximum amount of oxygen added at 120° is 880 millimoles/mole, then at 130° the maximum amount was 1200 millimoles/mole.

TABLE 3

Kinetics of the oxidation of polyisobutylene at various temperatures

110°		120°		130°	
Time of oxidation (hours)	Consumption of oxygen (millimol/mol.)	Time of oxidation (hours)	Consumption of oxygen (millimol/mol.)	Time of oxidation (hours)	Consumption of oxygen (millimol/mol.)
7	5.9	2.75	9.0	1.50	19.3
9	29.4	5.92	49.7	3.50	106.0
13	41.0	8.92	126.5	5.50	230.0
18	76.5	11.92	176.5	7.50	336.0
21	94.0	21.67	375.0	9.50	415.0
28	135.0	28.50	480.0	12.50	540.0
33	198.0	33.50	560.0	14.50	655.0
39	258.0	36.50	630.0	16.75	705.0
43	300.0	40.50	660.0	18.25	770.0
48	312.0	46.00	755.0	21.00	860.0
51	352.0	49.00	795.0	24.00	935.0
54	386.0	52.68	840.0	27.58	1030.0
57	397.0	55.92	870.0	30.58	1045.0

TABLE 4

Amount of acids in the volatile products of the oxidative cleavage of polyisobutylene (temperature 130°)

No.	Time of oxidation (in hours)	Amount of acids, calculated at HCOOH (in %)
77	4.0	7.2
74	6.0	8.4
82	13.0	11.9
86	18.5	10.9
87	47.0	12.0

Fig. 7 shows the decrease in molecular weight of polyisobutylene during oxidation at various temperatures.

The following conclusions can be drawn from the curves in Figs. 6 and 7: 1) at all oxidation temperatures the destruction of the polymer is completed in the earlier stages of the oxidation; 2) the amount of destructive cleavage increased with the increase in the temperature. The cleavage, especially, increased at temperatures over 120°.

In the early stages of absorption of oxygen, the molecular weight of the polyisobutylene decreased so much, that the polymer no longer had technical value.

TABLE 5

Change in unsaturation in the oxidation of polyisobutylene.

No.	Temperature	Time of oxidation	Iodine number
94	130°	0	0
95	130	1.0	16.2
92	130	6.0	28.5
83	130	18.5	13.7
90	130	48.0	50.8
101	120	6.0	12.5

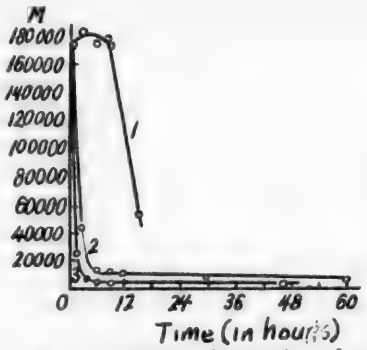


Fig. 7. Oxidative destruction of polyisobutylene at various temperatures. 1) 110°; 2) 120°; 3) 130°; M - molecular weight.

TABLE 6

Consumption of the inhibitor in the oxidation of butyl rubber at 130°. Initial concentration of the inhibitor was 25 millimoles/liter.

Elapsed time (in hours)	Free inhibitor (in %)
0	100.1
2	95.1
10	78,7
20	70.9
30	75.0
40	78.6
50	71.5
70	67.5
80	62.3

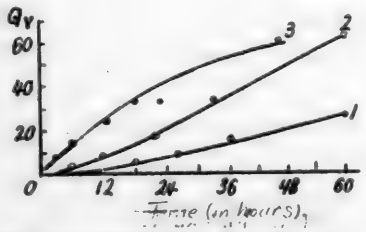


Fig. 8. Separation of the volatile reaction products during the oxidation of polyisobutylene at various temperatures. 1) 110°; 2) 120°; 3) 130°; Q_V - amount of volatile reaction products of the oxidation (in %).

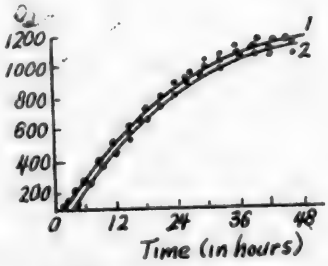


Fig. 9. Oxidation of polyisobutylene of various molecular weights at 130°. 1) Polyisobutylene molecular weight 175,000; 2) polyisobutylene molecular weight 50,000; O_2 - the amount of added oxygen (in millimoles/mole.).

Fig. 8 contains the results of the separation of volatile products in the reactions at various temperatures. The rate and the total amount of volatile products increased with the increase in temperature. Water, aldehydes, and ketones were detected in the volatile products. Characteristic results for the amount of acids formed in various stages are given in Table 4. Usually the sum of the acids formed, at the various stages of the oxidation of polyisobutylene, is around 8-12%. The amount of acids in the oxidized polymer is about 3-5%.

Only traces of peroxides were found in all the stages of the oxidation. Apparently the peroxides of polyisobutylene are unstable at higher temperatures and quickly decompose. The unsaturation of polyisobutylene is increased during the process of its oxidation (Table 5).

In a separate series, the effect of the molecular weight of isobutylene upon the kinetics of its oxidation was studied. The results of the experiments are given in Fig. 9. The kinetic oxidation curves of two forms of polyisobutylene, one of which had an average molecular weight of 50,000 and the other 175,000, are given in the figure. Both of the curves coincide satisfactorily, so that it can be said that the molecular weight of the polymer has no effect on the autocatalytic oxidation.

When polyisobutylene was heated in high vacuum, cross-linking occurred, as is shown by Figure 10.*

* The investigation of the structural changes in polyisobutylene and butyl rubber in high vacuum were conducted by A.S.Kuzminsky and I.A.Shokinim.

TABLE 7

Kinetics of the oxidation of butyl rubber at 110°

Elapsed time (in hrs.)	Oxygen consumption (in millimoles/mole)	Elapsed time (in hrs.)	Oxygen consumption (in millimoles/mole)
5.0	10.0	11.0	70.0
6.0	15.0	12.0	85.0
7.0	25.0	15.0	112.0
8.0	40.0	17.0	132.0
9.0	50.0	21.0	173.0
10.0	60.0	–	–

Oxidation of Butyl Rubber.

Figure 11 and Table 6 contain the results of the change of consumption of inhibitor in the oxidation of butyl rubber.

The curve for the consumption of the inhibitor in butyl rubber consists of two parts, AB and BC. The initial consumption is characterized by its great rapidity (part AB) but on part BC, the consumption rate of the inhibitor decreases. The autocatalytic oxidation of butyl rubber, like polyisobutylene, occurs with great rapidity.

The corresponding results are given in Figure 12 and Table 7.

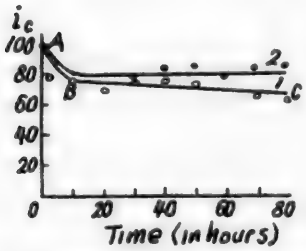


Fig. 11. Kinetics of the consumption of inhibitor in the oxidation of polyisobutylene and butyl rubber at 130°. 1) Butyl rubber; 2) polyisobutylene; i_c - inhibitor (in %).

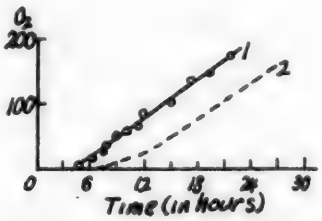


Fig. 12. Kinetics of the autocatalytic oxidation of butyl rubber and and polyisobutylene at 110°. 1) Butyl rubber; 2) polyisobutylene; O_2 - the amount of added oxygen (in millimoles/mole).

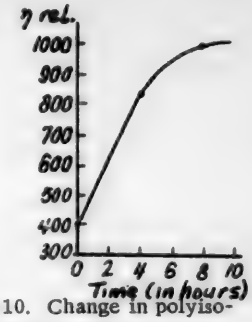


Fig. 10. Change in polyisobutylene in high vacuum at 200°. η_{rel} - the relative viscosity of benzene solutions of polyisobutylene.

As with polyisobutylene, when butyl rubber is heated in a high vacuum, cross-linking occurs.

Discussion of the Results

1. Oxidation of polyisobutylene. As shown in the experimental section, the consumption of the inhibitor occurs at the same time as the molecular weight of the polymer decreases wherein both proceed to a certain limit which varies with the temperature. Therefore, study of the inhibited oxidation of polyisobutylene leads to the conclusion that the long chains of the polymer are more reactive than the short. Oxidation of the polymer, in the presence of the inhibitor, apparently depends on the formation of peroxide radicals by the thermal decomposition of the high molecular weight fraction, and their subsequent extinction by reaction with the inhibitor. The free development of the reaction chain rapidly leads to an extensive destruction of the polymer.

An outline can be given for the initiation of the oxidation of polyisobutylene, which shows that the molecule splits and oxidizes to form peroxides. The peroxide radical, which forms as a result of the reaction, is the initial active center for the oxidation of polyisobutylene. The rate constant for the initiation of oxidation reaction of polyisobutylene (K_i), calculated from the results with the inhibitor, is equal to $1.8 \cdot 10^{-9}$ mole/liter/sec. at 110°.

If in unsaturated polymers the initiation rate constant is fully dependent upon the number of more active double bonds, which are located in the main chains of the molecule, then the value of K_i for polyisobutylene is determined by the molecular weight. As was pointed out above, the longer chains of polyisobutylene are less stable, react more easily, and as a result form the initial active centers which take part in the further development of the reaction chain. The weakness of the C-C bond in the molecular chain of polyisobutylene is the reason for its ease of oxidation.

Polyisobutylene is the most reactive of all of the saturated polymers. The ease of thermal and oxidative destruction of polyisobutylene does not allow the vulcanization of its peroxides necessary to change it to a polysilicone polymer. Conditions must be chosen for the vulcanization so that a considerable splitting of the molecule chain does not occur at the same time as the oxidation of the side methyl groups.

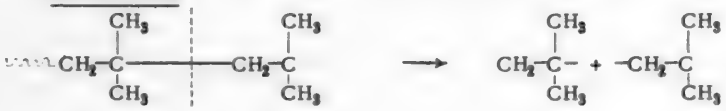
It can be shown that, in contrast, the value of the initiation constant, does not have an important effect on the kinetics of the autocatalytic oxidation. However, no real contrast exists as the free and inhibited oxidations proceed by different mechanisms. Upon comparing the curves of the decrease in the molecular weight with the curve for the separation of the volatile products, it can be pointed out that the oxidative process is accompanied by rupture of the chain of the polyisobutylene. At the beginning of the oxidation the molecular weight is decreased 10 times (from 175,000 to 2000-5000). The further destruction of the polymer is characterized by the extensive separation of volatile products so that, at the end of the experiment, 60% of the oxidized polymer goes into the gaseous phase.

At temperatures below 100° the polymer was oxidized extremely slowly. A measurable oxidation begins at 110°. The temperature coefficient of the rate of splitting, in the 110-120° range, is equal to 3. At temperatures above 120°, the oxidative splitting occurs with an extremely small temperature coefficient (1.1 − 1.2), which is characterized by a small energy of activation.

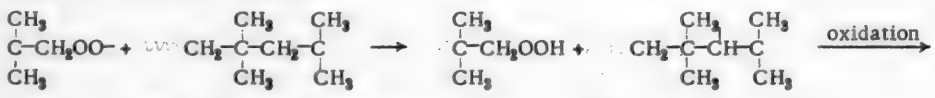
On the basis of the above experimental material, a probable outline for the oxidation of polyisobutylene was constructed.

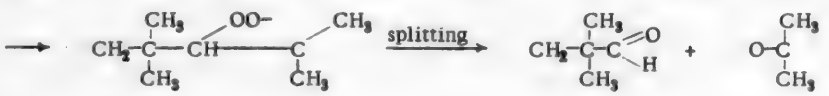
Schema of the oxidation of polyisobutylene

Initiation



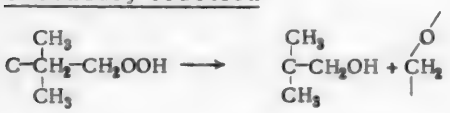
Development of the chain





Breaking of the chain

Secondary reaction



and so on according to the first chain of the scheme

The initial step of the oxidation is the formation of the peroxide radical.

The stabilization of the peroxide is undoubtedly related to the ortho-hydrogen atom of the methylene or methyl group, which, apparently, is related to the double bond formation.

2. Oxidation of butyl rubber. Butyl rubber has the properties of an unsaturated polymer and polyisobutylene. Like polyisobutylene it tends to be decomposed by heating, but its molecule contains double bonds in its main chain, which readily take part in initiation acts. Therefore, on the thermal oxidation of butyl rubber, the initial active centers will be formed by two processes: 1) by the splitting of the C–C bonds of the molecular chain, and 2) by the action of the oxygen on the double bonds of the polymer.

As shown in the experimental section, the curve for the consumption of the inhibitor consists of two parts. The beginning of the initiation occurs with great rapidity (part AB of the curve); it includes the active centers resulting from the rupture of the C–C bonds, and small amounts of those resulting from the addition of the oxygen to the double bonds. When a stable chain length of the molecule is reached, the further formation of initial active centers occurs only as a result of a thermal activation of the double bonds. Because of this, initiation for butyl rubber is characterized by two, not one, initiation constants:

K_r – the rate initiation constant of the process which proceeds by means of the C–C bonds; K_i – the rate initiation constant for the process occurring by means of the double bonds.

Calculated * from the results of the inhibited runs, the rates of the initiation of the oxidation of butyl rubber at 130° are respectively (in moles/liter/sec.):

$$K_r = 1.06 \cdot 10^{-7} \text{ and } K_i = 0.14 \cdot 10^{-7}.$$

K_i for butyl rubber is 35 times smaller than for sodium butadiene rubber. Because of this, it is the most stable of the unsaturated polymers.

It is clear that at lower temperatures, where the thermal decomposition does not as yet take place, it will be stable in relation to the degree of unsaturation. At temperatures over 100° active centers form, determined mainly by the value of K_r, which is 7 times greater than K_i.

This does not mean that ordinary bonds, at temperatures above 100°, become less stable than the π-component of the double bond. Apparently, the amount of ordinary bonds in butyl rubber exceeds the amount of double bonds 50 times, and the rate of the oxygen process is only 7 times greater than the first. Thus, it can be concluded that the rate of attack by the oxygen on the C–C position is 50:7 = 7.1 times slower than for the double bond position. As the chain length decreases, the process occurring by means of the C–C bonds decreases in rate and finally, at a certain chain length, it stops.

SUMMARY

1. The kinetics of the inhibited and autocatalytic oxidation of polyisobutylene and butyl rubber were studied at the temperature of 110-130°.

2. It was shown that the consumption of the inhibitor occurs concurrently with a decrease in the molecular weight of the polyisobutylene. Both of the processes occur at the same level varying with the temperature) only in the early stages of the reaction. On the basis of the above facts, it was concluded that the higher molecular weight fractions were more reactive than the lower molecular weight ones.

3. It was shown that the initiation of the oxidation of polyisobutylene occurred with the thermal cleavage of the molecular chains, which were in the high molecular weight fractions.

The initiation with butyl rubber depended as much on the rupture of the C–C bonds as on the oxidation of the double bonds. Therefore, the rate of initiation is not determined by one, but by two constants (at 130°; K_r = 1.06 mol/liter/sec; K_i = 0.14 mol/liter/sec).

4. It was shown that the free development of the oxidative process leads to a deep destruction of polyisobutylene in the early stages of the oxidation.

5. A probable schema for the reaction mechanism is given.

6. It was shown that both polyisobutylene and butyl rubber form cross-linkages when heated in a high vacuum (with a slight concentration of oxygen).

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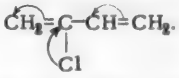
* K_i was calculated from the rate of the consumption of the inhibitor on the section BC of the curve. $K_i + K_r$ was calculated from the rate of consumption of the inhibitor on the section AB.

ACTION OF CHLOROAMIDES ON CHLOROPRENE IN AQUEOUS AND ALCOHOLIC SOLUTIONS

A. A. Petrov

Addition reactions of chloroprene, as additions between the conjugate double bond systems and polar substituents, are of great interest for the development of theories on the transformation of unsaturated compounds. The experimental material, up to now, shows the presence of radical differences in the additions of halogens, hydrogen halides, and hypohalous compounds to this substance. Chlorine adds more than 80% to the 1,4-positions of chloroprene [1], and bromine gives the 1,4 product almost exclusively [2]. Hydrogen bromide and chloride also add to the 1,4 positions to form the 4-halo-2-chlorobut-3-enes [3].

These results upheld the usual electronic formula of chloroprene; i.e., they indicated that a higher electron density was present at the first and a lower one at the fourth carbon atom:



However, with hypohalous compounds, especially with hypobromous acid [4] and alkyl hypoiodides [5], chloroprene gives almost exclusively 3,4-products. Chlorine iodide behaves in a similar way [6]. In this case, the greatest electronic density is found on the 4th carbon atom, which disagrees with the electronic theory. Therefore, it must be admitted that the order of addition is not determined, in this case, by the resulting polarization of the molecule, but by the mutual interaction of the molecules at the moment of the reaction. In relation to the preferred addition of hypohalous compounds to neighboring carbon atoms, chloroprene is not an exception. This order of addition has been found for hypohalous compounds in all experiments up to now.

The author, for example, showed that with divinyl, the ratio between the 1,2- and 1,4-products with hypochlorites, depends on the nature of the starting compound and the molecule which is adding, as well as on the temperature of the reaction system [7]. With alkyl hypobromites and alkyl hypoiodites, the formation of 1,4-compounds could not be shown in any of the cases studied [7,8].

On continuing the study of the reactions of chloroprene with hypohalous compounds, the author found that, in spite of the established rule, hypochlorous acid and alkyl hypochlorites added to chloroprene preferentially at the 1,4 positions, when aqueous or alcoholic solutions are treated with chloroamides *. Therefore, this was the first case to be found where hypohalous compounds added preferentially to the ends of a conjugated system.

Chloroprene chlorhydrin was obtained by the action of an aqueous solution of mono chlorourea in acidic media. Theoretically the six following compounds could be expected to form: five of them, chloroalcohols; one, the unsaturated chloroketone. The latter was previously obtained by the cleavage of bromine from the oxidation product of divinyl dibromide chlorohydrin [8].

$CH_2Cl{-}CCl(OH){-}CH{=}CH_2 \longrightarrow CH_2Cl{-}CO{-}CH{=}CH_2$ (I);
$CH_2Cl{-}CCl{=}CH{-}CH_2OH$ (II); $CH_2OH{-}CCl_2{-}CH{=}CH_2$ (V);
$CH_2{=}CCl{-}CHOH{-}CH_2Cl$ (III); $CH_2{=}CCl{-}CHCl{-}CH_2OH$ (VI):
$CH_2OH{-}CCl{=}CHCl$ (IV);

Distillation of the reaction products showed that, mainly, two substances were formed. The first of these, (chlorohydrin III) was extracted with water from the substances in the lower boiling fraction. The second (chlorohydrin II) was obtained in almost pure state by a simple distillation of the reaction products. The unsaturated chloroketone, which could easily be detected by its sharp odor, was not found in any quantity.

Besides the two chlorohydrins considerable amounts of products, resulting from the addition of chlorine to the chloroprene, and undistillable substances which were not investigated further, were obtained.

* The question of the mechanism of the reaction between chloroamides and olefins in aqueous and alcoholic solutions was studied in previous investigations [7].

The usual yield of the chlorohydrin was about 30%. The ratio between the first (Formula III) and the second (Formula II) chlorhydrin was 1:2.6 for the three experiments. The structure of the chlorohydrin, b.p. 75.5-76° at 20 mm, was determined by the method used previously to determine the structure of chloroprene bromohydrin [4]. The presence of the hydroxyl group was shown by acetylation with acetic anhydride. The acetate was obtained in 80% yield. The presence of a double bond was shown by bromination in chloroform with bromine. The reaction proceeded very easily and produced a liquid dibromide. The bromohydrin of similar structure gave a crystalline. The position of the hydroxyl group was determined by the oxidation of the bromide to the ketone, which gave methyl ethyl ketone upon reduction with zinc and acetic acid. Therefore, the hydroxyl group undoubtedly was tertiary in character and so only Formula (III) could be assigned to it. All of the other formulas were excluded. In connection with this formula, chlorohydrin (III) formed the previously studied chloroprene oxide by the action of bases.

The structure of the chlorohydrin, b.p. 114.5-115° at 20 mm, was determined in the following manner. The presence of a hydroxyl group was shown by acetylation with acetic anhydride which, because it was a primary hydroxyl group, went very easily. The yield of the acetate was about 90%. The acetate was easily differentiated from that of chlorohydrin (III) by its odor. The presence of a double bond was shown by bromination. The bromine added to this compound with difficulty. The reaction was not completed even after 24 hours. The yield of the dibromide was about 80%. No ketone was formed by the oxidation of this compound with the chromic mixture. Monochloracetic acid was obtained in good yield upon oxidation of the chlorohydrin with potassium permanganate. The formation of the latter is possible only with chlorohydrins (II) and (IV).

TABLE 1

Substance	Boiling point	Pressure (in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated
$CH_2=CCl-CHOH-CH_2Cl$	75.5-76	20	1.3126	1.4916	31.14	31.46
$CH_2=CCl-CH(OCOCH_3)-CH_2Cl$	89-89.5	20	1.2443	1.4650	40.68	40.83
$CH_2Br-CClBr-CHOH-CH_2Cl$	134.5-136	10	2.1002	1.5701	47.00	47.46
$CH_2Br-CClBr-CO-CH_2Cl$	124-125	10	2.0991	1.5600	46.04	45.85
$CH_2Cl-CCl=CH-CH_2OH$	114.5-115	20	1.3323	1.5100	31.66	31.46
$CH_2Cl-CCl=CH-CH_2OCOCH_3$	116.5-117	20	1.2646	1.4822	41.28	40.83
$CH_2Cl-CClBr-CHBr-CH_2OH$	142.5-143	10	2.0973	1.5740	47.33	47.46

The choice between these formulas, in favor of Formula (II) was based on the fact that two atoms of chlorine were removed by the action of zinc on the chlorohydrin in aqueous alcohol. The corresponding alcohol could not be isolated, but ethers of 1,2-butadien-4-ol could be obtained from the ethers of this chlorohydrin (see below). Therefore, formula II was adopted for the chlorohydrin by analogy with the structure of these ethers.

Table 1 contains the constants of the chlorohydrins and several of their derivatives.

A comparison of the constants of chlorohydrins (III) and (II) with the constants of analogously formed divinyl chlorohydrins, led to the following generalizations: in the case of 1,4-derivatives, as a rule the value of the molecular refractivity found is greater than the value calculated; in the case of the 1,2-derivatives, the calculated value of the molecular refractivity, as is usual for many organic compounds, is greater than that found. The presence of an exaltation with the 1,4-derivatives must be related to the decreased reactivity of the double bond in these compounds. It is also interesting to point out that the 1,4-chlorohydrin of chloroprene boiled higher than the 3,4-bromohydrin of chloroprene.

An outline of the method for the determination of the structure of the products of the reaction between chloroprene and an aqeuous solution of monochlorourea is given below. (see next page)

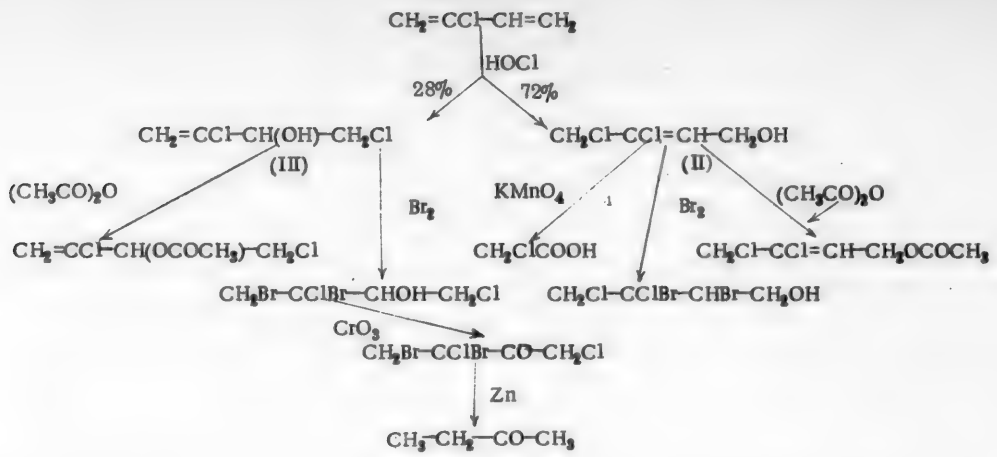
Two of the six possible chloroethers were obtained in each case by the action of N,N-dichlorophenylsulfonamide on solutions of chloroprene in methyl and ethyl alcohols.

$CH_2Cl-CClOR-CH=CH_2$ (I) $CH_2Cl-CCl=CH-CH_2OR$ (II) $CH_2=CCl-CHOR-CH_2Cl$ (III)

$CH_2OR-CCl=CH-CH_2Cl$ (IV) $CH_2OR-CCl_2-CH=CH_2$ (V) $CH_2=CCl-CHCl-CH_2OR$ (VI)

Besides the chloroether, the reaction products also included 1,2-dichloro-1,3-butadiene, chloroprene dichloride, and a very small amount of an undetermined chloroketone, formed, apparently, as a result of

Schema 1



the hydrolysis of the chloroether with Formula (II) during steam distillation of the reaction products. The formation of 1,2-dichlorobutadiene indicates that chloroprene, like benzene, can enter into substitution reactions. Small amounts of 1,2-dichlorobutadiene [1] were also formed during the chlorination of chloroprene.

The lower boiling chloroethers could not be separated from the dichlorides by distillation. They were purified, either by treatment with alcoholic alkali in the cold, or by the action of zinc dust in a heated aqueous alcoholic solution. In comparison, chloroethers were more stable than the dichloride to these reagents.

The higher boiling chloroether, which constituted about 80% of the mixture of chloroethers, was isolated in a substantially pure state by the usual vacuum distillation through a column.

The yield of the chloroethers was usually around 50%. This appeared to be the usual yield of the chloramide method.

The structure of the chloroethers was determined in the same manner as the structures of the ethers of chloroprene iodohydrin had previously been [5]. Previously reported chloralkoxyprenes, whose structure had been determined by their transformation (action of dilute H_2SO_4) into ketones which, by bromination and then reduction, were transformed into methyl ethyl ketone, obtained by warming them with alcoholic alkali. Therefore, of all the possible formulas, only formula (III) could be assigned to this substance.

Determination of the structure of the higher boiling chloroether presented greater difficulties. However, they were eliminated and a method for structure determination was found. A mixture of monochloroacetic acid and ethoxy acetic acid was obtained by the oxidation of the substance with potassium permanganate; the former in a much greater amount. This transformation made it possible to assign either Formula (II) or (IV) to the chloroether. In order to resolve this question of the structure, after a study of a series of other possibilities, the property of aliphatic dihalides containing neighboring halogen atoms, that their halogens were removed with zinc to form ethylene derivatives [10], was employed. If the halogen atoms are not side by side, the zinc reacts slowly and usually a substitution of the halogen by hydrogen occurs. The chloroethers reacted very rapidly with zinc dust in aqueous alcohol solutions to form allenic ethers, one of which had already been reported in the literature [11] as the main reaction product The formulas of these ethers corresponded with the analysis. A comparison of their constants with those of isomeric butadiene ethers, which have been fully described in the literature of the last few years, made it possible to assign to them the formula given in the outline, which was based on their method of preparation.

Besides the allenic ethers, the action of zinc on the chloroethers produced the previously described ethers of chlorocrotonyl alcohol [3]; i.e. a large amount of the more active chlorine atom was reduced. The formation of similar side products has been frequently reported in the literature. Chloroprene was another side product. The yield of chloroprene was sharply reduced upon going from methyl to ethyl, to butyl ethers. The formation of chloroprene can be explained by the 1,4-elimination of the halogen and the alkoxyl group.

Therefore, no indication of the presence of other substances, outside of the chloroethers of Formula (II), in the higher boiling fraction of the chloroethers was obtained. The homogeneity of the ethers was also shown by their narrow range boiling points. It also must be pointed out that chloroethers of the Formula (III) slowly eliminated chlorine and the alkoxyl, under the same conditions, to form chloroprene.

It was necessary to find out, whether or not the unsaturated ketone – the product of the hydrolysis of the chloroether of Formula (I) – was present in small quantities in the lower boiling fractions of the reaction products. The sharp odor of this ketone (characteristic for unsaturated ketones) would have been the first evidence of its presence in the lower fractions. Analysis of the fraction, corresponding in boiling point to the unsaturated ketone, (less than 2% of the mixture of the chloroethers) showed that it contained a large amount of a substance richer in chlorine. However, this fraction gave a crystalline compound with p-nitrophenylhydrazine. This showed beyond doubt that a carbonyl compound was present. That this compound was a ketone was shown in the following manner. The whole of the narrow fraction was brominated and the bromides were reduced with zinc turnings in acetic acid. Then a portion, boiling up to 100°, was distilled from the reaction product. The presence of methyl ethyl ketone was shown in the distillate (test with p-nitrophenylhydrazone).

Table 2 contains the constants of the ethers obtained.

TABLE 2

Substance	B.p.	Pressure (in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated
$CH_2=CCl-CHOCH_3-CH_2Cl$	58-59°	20	1.1710	1.4612	36.37	36.20
$CH_2=CCl-CHOC_2H_5-CH_2Cl$	67.5-68	20	1.1297	1.4562	40.89	40.82
$CH_2Cl-CCl=CH-CH_2OCH_3$	80-81	20	1.2177	1.4788	36.09	36.20
$CH_2Cl-CCl=CH-CH_2OC_2H_5$	90-90.5	20	1.1683	1.4734	40.62	40.82
$CH_2Cl-CCl=CH-CH_2OC_4H_9$	119-120	20	1.0883	1.4672	50.27	50.05
$CH_2Cl-CClBr-CHBr-CH_2OC_2H_5$	127-129	10	1.8134	1.5312	56.12	56.82

TABLE 3

Substance	B.p. (at 755-760 mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Literature reference
$CH_2=C=CH-CH_2OCH_3$	87.5-87.8	0.8327	1.4395	26.60	26.00	–
$CH_2=C=CH-CH_2OCH_3$	87-89	–	–	–	–	[11]
$CH_2=C=CH-CH_2OC_2H_5$	107.5-107.8	0.8228	1.4389	31.36	30.62	–
$CH_2=C=CH-CH_2OC_4H_9$	153.5-154	0.8270	1.4432	40.47	39.85	–
$CH\equiv C-CH_2-CH_2OC_2H_5$	104	0.8273*	1.4148*	29.73	29.49	[12]
$CH_3-C\equiv C-CH_2OC_2H_5$	119-120	0.8363	1.4290	30.25	29.49	[13]
$CH_2=CH-CH=CHOC_2H_5$	37-38 (at 41 mm)	0.8205	1.4671	33.19	30.19	[14]

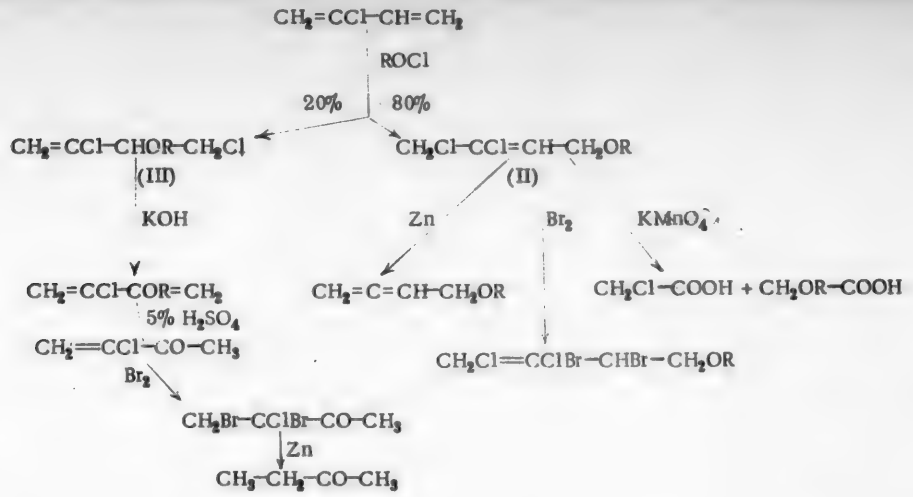
In contrast to the chlorohydrins, the 1,4-chloroethers do not give exaltations in the molecular refractivity, even though the double bonds are less reactive than in the chlorohydrins.

Table 3 lists the constants of the allenic ethers. The constants are given in this table for all of the isomeric primary ethyl ethers obtained up to now. It is seen from this table, that the highest boiling points and densities are given by ethers of acetylenic alcohols with a central triple bond. The largest refractive index is given by the conjugated diene ether. This ether gives a considerable amount of exaltation in the molecular refractivity. The great differences in the values of the refractive indices of the isomeric ethyl ethers are outstanding. The same properties were found for the methyl ether series.

An outline for the determination of the structure of the chloroethers formed by the action of the dichloroamide on chloroprene, in alcoholic solutions, is given below: (see top of next page)

In conclusion, it is necessary to discuss certain theoretical considerations relating to the properties found. From the results of the above studies, it was, first of all shown that the point of the initial attack in the reaction

* At 22°



between chloroprene and the hypohalous compounds depends on the nature of the halogen. The first carbon atom served as the initial point of attack with hypochlorous acid, and the reaction was completed at the 4 position. Thus the chloroprene molecule reacted as a conjugated system. With hypobromous acid and with hypoiodite esters, the initial point of attack was the 4 carbon atom, and the reaction was completed at position 3. A conjugated system was not present. The addition occurred at the unsubstituted, more reactive, double bond.

Therefore, the addition of hypochlorites occurred in the same manner as the addition of the halides. The order of addition for hypobromous and hypodiodous compounds was different from the order of the addition of the halides. Chlorine iodide added in the same order as the hypoiodous compounds. This new property can be explained by the presence of steric hindrance to the addition of bromine and iodine to the first position. Since position one is hindered, these halides added instead to the unsubstituted double bond.

It can be supposed that chloroprene can polarize like a conjugated system, in the presence of the poles of the corresponding hypochlorite compound, to give the maximum electron density at position one. This results in 1,4-addition. With hypobromous and especially hypoiodous compounds, this polarization does not occur, and the addition proceeds in the same manner as in a system of two isolated double bonds, one of which is more active than the other; 3,4-addition results.

It must be pointed out that the results of the hypochlorination of chloroprene are new experimental proofs of the ability of conjugated systems to add 1,4 preferentially. In fact, in the case of chloroprene, the 1,2 addition cannot occur at all and therefore cannot be the source of the 1,4 product.

EXPERIMENTAL

Action of an aqueous solution of monochlorurea on chloroprene. Freshly distilled chloroprene (177 g – (two-fold excess) was shaken for 1 hour, with cooling (until ice crystals formed) and acidification with H_2SO_4 (until 2% H_2SO_4 content), with a solution of monochlorurea, obtained by passing chlorine at –10–0° into a solution of 60 g of urea in 450 ml of water with 60 g of copper carbonate until an increase in weight of 50 g, and almost complete solution of the copper carbonate occurred. The oil was separated from the aqueous solution, dried with Na_2SO_4, and distilled, at first in a slight vacuum, and then at 20 mm. A small amount of the reaction products was extracted from the water and added to the main part of the substances. Results of the distillation:

1) 55-65° –70 g; the rest at 20 mm: 2) to 70° –4.0 g; 3) 70-80° –28.8 g; 4) 80-110° –5.4 g; 5) 110-120° –32.0 g; 6) 120-140° –4.5 g; 7) nondistillable residue –45 g.

The first fraction was unreacted chloroprene. The third fraction, according to analysis for chlorine, consisted of chloroprene chlorohydrin considerably contaminated with dichlorides. The chlorohydrin was extracted from this fraction with water. 27.8 g of the 70-80° fraction and 700 ml of water (100 ml portions) were used for the extraction. The last extraction did not give any decrease in the weight of the oil, which was equal to 15.1 g. Analysis of the residual oil for chlorine and determination of its constants showed that chloroprene

dichloride was being dealt with.

B.p. (main part 67-69° at 10 mm; n_D^{15} 1.5145. 0.1546 g substance: 0.4136 g AgCl. Found %: Cl 66.18. $C_4H_5Cl_3$. Calculated %: Cl 66.73.

The following constants were obtained for chloroprene 1,4-chlorohydrin: b.p. 67-69° at 10 mm, n_D^{15} 1.5121.

9.7 g of the chlorohydrin (III), which distilled almost completely over a 1° range, was extracted from the aqueous solution after saturation with salt. The constants for the substance are given in Table 1.

0.1904 g substance: 0.3886 g AgCl. 0.1844 g substance: 0.3728 g AgCl. Found %: Cl 50.49, 50.01 $C_4H_6OCl_2$. Calculated %: Cl 50.29. A redistillation of the fifth fraction resulted in 26.5 g of a substance, b.p. 114-116° at 20 mm, the main part of which had the constants given in Table 1. This fraction was shown, by analysis for chlorine, to be pure chloroprene chlorohydrin (III).
0.1572 g substance: 0.3198 g AgCl. Found %: Cl 50.32. $C_4H_6OCl_2$. Calculated %: Cl 50.29.

The nondistillable residue was a tar-like mass. Its nature was not investigated further.

Thus 35.2 g of the pure chlorohydrins (III) and (II) or 25% of theory was obtained from 1 mole of monochlorurea. The ratio between the amount of the chlorohydrin (III) and (II) was 1:2.6. If the amount of the chlorohydrins in the intermediate fractions was taken into account, the yield would be about 30%.

The acetylation of the chlorohydrins was effected with the aid of 150% acetic anhydride and a drop of H_2SO_4. When the H_2SO_4 was added, the reaction mixture was cooled to keep the temperature from exceeding 40°. The yield of the acetate of chlorohydrin (III) was 82% and that of (II), 89%. The constants of the acetates are given in Table 1.

Chlorohydrin (III) acetate: 0.1610 g substance: 0.2552 g AgCl. Found %: Cl 39.21. $C_6H_8O_2Cl_2$. Calculated %: Cl 38.74.

Chlorohydrin (II) acetate: 0.1352 g substance: 0.2908 g AgCl. Found %: Cl 38.84. $C_6H_8O_2Cl_2$. Calculated %: Cl 38.74.

Chlorohydrin (III) acetate has a more intense pleasant odor.

Bromination of the chlorohydrins was effected with equivalent amounts of bromine in chloroform. Chlorohydrin (III) added bromine readily; decolorization of the solution occurred in a few minutes and was accompanied by the evolution of heat. A yield of 13.5 g −82% of the bromide was obtained from 7.7 g of the chlorohydrin.

0.1950 g substance: 0.4312 g AgCl + AgBr. Found %: Cl + Br 77.05. $C_4H_6OCl_2Br_2$. Calculated %: Cl + Br 76.70.

Chlorohydrin (II) added bromine slowly; decolorization of the solution occurred only on the next day. A 7 g −78% yield −of the dibromide was obtained from 4.2 g of chlorhydrin (II).

0.1646 g substance: 0.3656 g AgCl + AgBr. Found %: Cl + Br 77.39. $C_4H_6OCl_2Br_2$. Calculated %: Cl + Br 76.70.

Both of the dibromides were viscous, slightly yellow liquids with a pinelike odor.

Oxidation of chlorohydrin (III) dibromide. 10 g of 80% H_2SO_4 was added dropwise, with mechanical stirring and cooling (15-20°), to a solution of 10 g of chlorohydrin (III) dibromide and 5 g of sodium dichromate in 30 ml of 80% acetic acid. After 2 hours of stirring, the mixture was diluted with water, the ketone was separated, washed with aqueous sodium carbonate, and dried with $CaCl_2$. The last operations were best conducted with a solution of the ketone in ether. A 8.7 g −88% yield, of the ketone was obtained. The constants are given in Table 1.

0.1889 g substance: 0.4200 g AgCl + AgBr. Found %: Cl + Br 77.47. $C_4H_4OCl_2Br_2$. Calculated %: Cl + Br 77.22.

The ketone was a yellow, lively liquid with a characteristic sour, somewhat irritating odor. It was easily reduced to methyl ethyl ketone with zinc in acetic acid. Methyl ethyl ketone was steam distilled from the

reaction mixture and analyzed in the distillate, as the p-nitrophenylhydrazone, m.p. 122-124°.

Oxidation of chlorohydrin (II). 29 g of potassium permanganate was added, in small portions over a 2 hour period with mechanical stirring and cooling (to 15-20°), to a mixture of 7.1 g of chlorohydrin (II), 20 g of magnesium sulfate, and 150 ml of water. After the filtration of the manganese dioxide, the solution was evaporated in vacuum until the beginning of crystallization, acidified with 5% H_2SO_4 and treated with ether until the extraction of acids ceased. After distillation of ether, chloroacetic acid, contaminated by a small amount of oxalic acid, from which it was purified by distillation, remained in the flask. The yield of the monochloroacetic acid was 3.5 g or 75%.

0.1828 g substance: 0.2779 g AgCl. Found %: Cl 37.61. $C_2H_3O_2Cl$. Calculated %: Cl 37.53.

Action of alkali on the chlorohydrins. The previously reported chloroprene oxide was obtained by the distillation of chlorohydrin (III) over KOH (the chlorohydrin was added dropwise to an 80% solution of KOH heated to 150°). The yield, from 5 g of chlorohydrin, was 3.0 g or 80%. B.p. 109-111°, n_D^{20} 1.4594. A b.p. of 109.4-109.6° and n_D^{20} 1.4592 was found previously for chloroprene oxide.

When chlorohydrin (II) was distilled over alkali under the same conditions, a tarring of the substance occurred. 0.5 g of a liquid distillate, n_D^{20} 1.4795, was obtained from 7 g of the chlorohydrin; it was not investigated any further.

Action of N,N-dichlorophenylsulfonamide on methyl alcohol solutions of chloroprene. 126 g of N,N-dichlorophenylsulfonamide (90% activity) was added in small portions, with mechanical stirring and cooling to a temperature of +4-6° with a freezing mixture to 132 g of freshly distilled chloroprene (several fold excess) in 300 ml of ethyl alcohol. The mixture was stirred for 1 hour after the addition of the chloroamide. A test with acidified KI solution showed that no active chlorine was present in the solution. The chloroethers were steam distilled until the oily droplets disappeared from the distillate. 75.8 g of phenylsulfonamide was extracted from the residue with hot water. There then remained 13 g of a tarry substance, which probably was the thermally changed addition products of chloroamide and chloroprene.

The reaction products, separated from unreacted chloroprene, were vacuum distilled at 20 mm:

1) to 50° –3.2 g; 2) 50-60° –19.0 g; 3) 60-70° –3.4 g; 4) 70-78° –2.1 g; 5) 78-83° –59 g; 6) 83-100° –3.2 g; 7) residue, 8 g.

Analysis of the 50-60° fraction showed that it consisted of a mixture of chloroprene chloroether and dichloride. To remove the dichlorides, the fraction was treated in the cold, with 10% alcoholic KOH until an alkaline reaction was obtained. 30% of the KOH, equivalent to one chlorine atom, was consumed. After such a treatment, the ether boiled over a narrower range (57-60° at 20 mm). However, it still contained some of the chloride.

0.1964 g substance: 0.3896 g AgCl. Found %: Cl 49.07. $C_5H_8OCl_2$. Calculated %: Cl 45.74.

This fraction was used for the determination of the structure of the main product without further purification.

The fraction was treated with zinc dust in aqueous alcohol for the preparation of the pure chloroether. After boiling for 30 min., the reaction products were steam distilled, separated, dried, and vacuum distilled. The substance with the constants given in the table was obtained in this manner.

0.1728 g substance: 0.3167g AgCl. Found %: Cl 45.34. $C_5H_8OCl_2$. Calculated %: Cl 45.74.

50 g of a substance, b.p. 80-81° at 20 mm, and other constants, given in Table 2, was obtained by the redistillation of the fifth fraction.

0.1822 g substance: 0.3420 g AgCl. Found %: Cl 46.43. $C_5H_8OCl_2$. Calculated %: Cl 45.74.

Thus, the total yield of the chloroethers, if the intermediate fractions were taken into account, was about 80 g or 52%. The ratio between chloroether (III) and (II) = 1:3.5.

Action of alcoholic alkali on the chloromethyl ether (III). 7.8 g of the chloromethyl ether (III) was added through the reflux condenser to a boiling solution of 5.6 g of KOH in 25% alcohol. After 30 minutes of refluxing, the reaction products were steam distilled. 4 g of chloromethoxyprene, b.p. (main fraction) 58-59.5° at 85 mm, d_4^{20} 1.0681, n_D^{20} 1.4732., was obtained. Previously the constants: b.p. 58.5-59.5°, d_4^{20} 1.0579, n_D^{20} 1.4712, were obtained for this substance. When the substance was hydrolyzed by shaking with 5%

When the substance was hydrolyzed by shaking with 5% H_2SO_4, the previously reported ketone, 38-40° at 30 mm, was obtained.

Action of alcoholic alkali on chloromethyl ether (II). 10.5 g of chloromethyl ether (II) was added in small portions to a solution of 4 g of NaOH in 25 ml of methyl alcohol, and the mixture was refluxed for 30 min. on the water bath. 4.3 g of NaCl, as compared to the calculated 4 g, precipitated. Upon distillation of the reaction mixture, 5 g of a substance, which boiled mainly at 68-72°, d_4^{20} 1.0228, n_D^{20} 1.4440, was obtained. The substance contained a lower percent of chlorine than was required for chloroerythroglycol dimethyl ether.

0.1475 g substance: 0.0958 g AgCl. Found %: Cl 16.07. $C_6H_{11}O_2Cl$. Calculated %: Cl 23.54.

Action of zinc on an aqueous alcoholic solution of the chloromethyl ether (II). Chloromethyl ether (II) was added, dropwise through the side arm, into a flask containing 30 g of zinc dust in 100 ml of 70% alcohol, while the mixture was being continuously distilled through a 30 cm herringbone dephlegmator. A violent reaction took place, forming substances which were readily separated from the distillate by mixing with a $CaCl_2$ solution. After separation of the reaction products, the solution was distilled once more, and some more of the substances were obtained from the first part of the distillate. A total of 17.2 g of an oil was obtained which, on redistillation through a 30 cm dephlegmator, was readily separated into the following fractions: 1) 55-65° —2.6 g; 2) 65-87.25° —2.1 g; 3) 87.25 —87.75° —62 g; 4) 87.75 —100° —1.0 g; 5) residue —3.6 g.

The first fraction was chloroprene. The characteristic condensation product, m.p. 173-175°, was obtained by heating the substance with a benzene solution of maleic anhydride in a sealed ampoule on the water bath, and processing it in the usual manner.

The third fraction was the allenic ether previously reported by Carothers. The constants for the substance are listed in Table 3. Analytical results: 0.1428 g substance: 0.3722 g CO_2; 0.1201 g H_2O. Found %: C 71.11; H 9.41. C_6H_8O. Calculated %: C 71.39; H 9.59.

The yield of the allenic ether was about 40%.

The residue of the redistillation was not investigated. By analogy with the residue of the redistillation of the corresponding allenic ethyl ether (see the following paragraph), it probably contained the methyl ether of chlorocrotonyl alcohol.

It must be pointed out that the chloroether (I) remained unchanged under these conditions.

Action of N,N-dichlorophenylsulfonamide on solutions of chloroprene in ethyl alcohol. 186 g of N,N-dichlorophenylsulfonamide was added to a solution of 250 g of chloroprene in 650 ml of 98% ethyl alcohol, under the conditions given above in the experiment with methyl alcohol. At the end of the addition, the mixture was stirred for 4 hours, after which a test with KI showed that only insignificant amounts of active chlorine were present. Upon distillation of the mixture of chloroethers and side products, the following fractions were obtained: 1) 47-49° at 85 mm —1.8 g; the rest at 20 mm: 2) to 60° —5 g; 3) 60-70° —26.5 g; 4) 70-80° —5 g; 5) 80-89° —5 g; 6) 89-91° —95 g; 7) 91-100° —5.8 g, 8) residue —10.5 g.

In addition, 119.1 g of the amide and 44 g of a residue, which did not steam distil, were obtained.

The first fraction was the previously reported 1,2-dichlorobut-1,3-dien: d_4^{15} 1.1993; n_D^{15} 1.5078.

0.1444 g substance: 0.3304 g AgCl. Found %: Cl 56.60. $C_4H_4Cl_2$. Calculated %: Cl 57.67.

Literature data: b.p. 46.75-47.5° at 85 mm; d_4^{15} 1.1992; n_D^{15} 1.5078.

The fraction possessed lachrymatory activity, which indicated that it contained the unsaturated chloroketone, $CH_2Cl{-}CO{-}CH{=}CH_2$. However, its constants and chlorine content differed widely from those of the ketone. A portion, corresponding to the unsaturated ketone by virtue of its b.p., was separated from this fraction. It had the following constants: b.p. 69-70° at 60 mm, d_4^{20} 1.2341, n_D^{20} 1.4788.

0.1520 g substance: 0.3256 g AgCl. Found %: Cl 52.99. C_4H_5OCl. Calculated %: Cl 33.92.

According to the literature, the unsaturated ketone has the following constants:

b.p. 70° at 60 mm; d_4^{20} 1.2604; n_D^{20} 1.4675.

The presence of the unsaturated chloroketone was shown, finally, by the preparation of crystalline derivatives with semicarbazide and p-nitrophenylhydrazine. The p-nitrophenylhydrazone charred at 110°.

The fraction was also treated with an excess of bromine in chloroform, and the product obtained, was boiled with zinc turnings in acetic acid for 30 minutes. It was distilled, and the portion boiled up to 100° contained methyl ethyl ketone, since it formed the characteristic p-nitrophenylhydrazone, m.p. 122-124°, with p-nitrophenylhydrazine in acetic acid.

The third fraction was a mixture of the chloroether (III) and chloroprene dichloride.

d_4^{20} 1.1814; n_D^{20} 1.4665. 0.1880 g substance: 0.3450 g AgCl. Found %: Cl 45.39. $C_6H_{10}OCl_2$. Calculated %: Cl 41.95.

If this substance did not contain any impurities other than the dichloride, then it was a mixture 86% chloroether and 14% dichlorides.

A purified chloroether was obtained by treatment with alkali.

B.p. 66-69° at 20 mm; d_4^{20} 1.1419; n_D^{20} 1.4588.

0.1566 g substance: 0.2774 g AgCl. Found %: Cl 43.82. $C_6H_{10}OCl_2$. Calculated %: Cl 41.95.

This product was used without further purification for determination of the structure of the chloroether (III). The pure chloroether (III) was obtained by treating the fraction with zinc dust in the same manner as in section 8. The constants are listed in Table 2.

0.1807 g substance: 0.3062 g AgCl. Found %: Cl 41.91. $C_6H_{10}OCl_2$. Calculated %: Cl 41.95.

The sixth fraction, on redistillation, gave 85 g of a substance, b.p. 90-90.5° and other constants listed in Table 2.

0.1596 g substance: 0.2404 g AgCl. Found %: Cl 42.59. $C_6H_{10}OCl_2$. Calculated %: Cl 41.95.

The analytical results showed that the fraction was almost pure chloroether (II). It was used for the structure determination without further purification.

Therefore, the yield of the chloroethers, if the intermediate fractions were taken into account, was 126 g or 50% of theory (calculated for 90% N,N-dichlorophenylsulfonamide).

The ratio of the chloroethers (III) and (II) = 1:4.

Action of alcoholic alkali on the chloroether (III). 10 g of the chloroether (III) was added through the reflux condenser to a solution of 7 g of KOH in 40 ml of ethyl alcohol. The mixture was refluxed for 1 hour on the water bath. The reaction products were steam distilled. In this way, 5.8 g of an oil (74% yield), a large part of which boiled at 74-75° at 85 mm, d_4^{20} 1.0155, n_D^{20} 1.4652 was obtained.

0.1652 g substance: 0.1802 g AgCl. Found %: Cl 26.98. C_6H_9OCl. Calculated %: Cl 26.74.

The constants: b.p. 74.5-75° at 85 mm, d_4^{20} 1.0152, n_D^{20} 1.4641.

The substance was easily hydrolyzed to a ketone with b.p. 38-40° at 30 mm.

Bromination of the chloroether (II). The chloroether (II) reacted very slowly with bromine. When 7.5 g of the chloroether and an equivalent amount of bromine were allowed to stand together, almost complete decolorization was obtained only after several days; hydrogen bromide was evolved. As a result of this reaction, after the removal of the chloroform, 8 g (55% yield) of a substance, whose constants are given in the Table, was obtained.

0.1540 g substance: 0.3064 g AgCl + AgBr. Found %: Cl + Br 69.32. $C_6H_{10}OCl_2Br_2$. Calculated %: Cl + Br 70.16.

Action of zinc on the chloroether (II) in aqueous alcohol. 45 g of the chloroether (II) was added, under the conditions given for the methyl ether, to 40 g of zinc dust in 150 ml of boiling alcohol. After processing the distillate in the usual manner, 20 g of a substance, which was separated into the following fractions, was obtained: 1) 55-56° –1.4 g; 2) 65-107° –2.0 g; 3) 107-108° –0.5 g; 4) 108-125° –1.0 g; the rest at 25 mm: 5) to 52° – 0.6 g; 6) 52-54° –2.0 g; 7) 54-70° –1.0 g; 8) residue –0.5 g.

The first fraction was chloroprene.

The third fraction—the ethyl ether of butadien-2,3. Yield ~42%. The constants for the substance are listed in Table 3. Analytical results: 0.2502 g substance: 0.6698 g CO_2; 0.2336 g H_2O. Found %: C 73.06; H 10.45. $C_6H_{10}O$. Calculated %: C 73.42; H 10.27.

The sixth fraction was the previously reported ether of chlorocrotonyl alcohol. The yield was about 6%. Found for it: d_4^{20} 0.9843, n_D^{20} 1.4405.

0.1706 g substance: 0.1822 g AgCl. Found %: Cl 26.42. $C_6H_{11}OCl$. Calculated %: Cl 26.34.

The sixth fraction was the previously reported chlorocrotonyl ether with b.p. 52.5-53.5° at 25 mm, d_4^{20} 0.9832, n_D^{20} 1.4395.

Oxidation of the chloroether (II). 38 g of potassium permanganate was added, in small portions with continuous stirring and water cooling to 15-25°, to a mixture of 17 g of the chloroether in 150 ml of water. The last portions of permanganate were decolorized slowly.

After processing in the usual manner, 8.8 g of acids was obtained. A large portion of this substance crystallized.

An analysis of the mixture showed that it consisted of 76.5% chloroacetic acid (yield 70%) and 22.5% of ethoxyacetic acid (yield 18%).

0.1631 g substance: 0.1892 g AgCl. Found %: $CH_2ClCOOH$ 76.48. 0.2249 g substance: 0.1140 g AgI (Zeisel). Found %: $CH_2(OC_2H_5)COOH$ 22.47.

The crystalline acid was filtered, recrystallized from water, and analyzed. M.p. 61°.

0.1742 g substance: 0.2626 g AgCl. Found %: Cl 37.29. $C_2H_3O_2Cl$. Calculated %: Cl 37.53.

In addition to the acids reported, oxalic acid was also formed during the oxidation (m.p. 189°).

Action of N,N-dichlorophenylsulfonamide on solutions of chloroprene in butyl alcohol. 94 g of liquid products, 76 g of the amide, and 26 g of chloroamide-chloroprene addition products were obtained by the action of 120 g of N,N-dichlorophenylsulfonamide on a solution of 130 g of chloroprene in 300 g of butyl alcohol. Two main fractions were obtained on the redistillation of the liquid products: (at 20 mm): 1) 85-90° —9 g; 2) 117-122° —55 g.

The analysis and the determination of the constants of the first fraction showed that it contained a considerable amount of products richer in chlorine than the chloroethers. Found: d_4^{20} 1.2137, n_D^{20} 1.4830.

0.1816 g substance: 0.3760 g AgCl. Found %: Cl 51.22. $C_8H_{14}OCl_2$. Calculated %: Cl 35.98.

This fraction was not investigated further.

A large part of the second fraction came over at 119-120° (20 mm) and had the constants given in Table 2. This fraction contains a somewhat lower percent of chlorine than is required for the chloroether. It could not be purified further.

0.1846 g substance: 0.2605 g AgCl. Found %: Cl 34.91. $C_8H_{14}OCl_2$. Calculated %: Cl 35.98.

Action of zinc on the chlorobutyl ether (II) in aqueous alcohol. 11.2 g of the allenic ether (yield 45%) and 3.9 g of chlorobutenol ether (13%) were obtained by the action of 40 g of zinc dust in 200 ml of ethyl alcohol (75%) on 39.5 g of chlorobutyl ether (II) (fraction 117-122° at 20 mm).

The constants of the allenic ethers are listed in Table 3. The analytical results are as follows:

0.1922 g substance: 0.5353 g CO_2; 0.1942 g H_2O. Found %: C 76.01; H 11.31. $C_8H_{14}O$. Calculated %: C 76.14; H 11.19.

The chlorobutenol ether boiled at 86-92° at 25 mm and had d_4^{20} 0.9656, n_D^{20} 1.4432.

0.1706 g substance: 0.1447 g AgCl. Found %: Cl 20.98. $C_8H_{15}OCl$. Calculated %: Cl 21.80.

The following constants were previously found for this ether: b.p. 86.75-88.5° at 25 mm, d_4^{20} 0.9595, n_D^{20} 1.4442.

SUMMARY

1. The action of an aqueous solution of monochlorurea on chloroprene was studied. The formation of two chlorohydrins: $CH_2=CCl-CHOH-CH_2Cl$ and $CH_2Cl-CCl=CH-CH_2OH$ in a ratio of 1:2.6 was obtained. The acetate, dibromide, and oxide were obtained from the first, and the acetate and dibromide from the second. The structure of the first chlorohydrin was determined by transforming it into methyl ethyl ketone, the structure of the second – by oxidizing it to monochloroacetic acid.

2. Two ethers in a ratio of 1:4, corresponding in structure to the two chlorohydrins listed above, were obtained in each case by the action of N,N-dichlorophenylsulfonamide on solutions of chloroprene in methyl, ethyl, and butyl alcohols. The structures of the lower boiling ethers were determined by transforming them into chloroalkoxyprenes; the structure of the isomeric chloroethers was determined by oxidizing them to monochloroacetic acid and reducing them to the allenic ethers.

3. The present investigation showed the presence of basic differences in the order of addition to chloroprene hypochlorous acid and its esters, and the addition of hypobromous acid hypoiodite esters.

The above differences are of considerable interest for theoretical organic chemistry.

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SYNTHESIS OF ALIPHATIC ORGANO-ELEMENTAL COMPOUNDS BY THE DIAZO METHOD

I. SYNTHESIS OF COMPOUNDS WITH THE GROUP V ELEMENTS — ORGANO-ANTIMONY, ARSENIC, AND BISMUTH COMPOUNDS

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The reaction between the metallic halides and the aliphatic diazo compounds was studied for $CuCl_2$, $CaCl_2$, $MnCl_2$, $MgCl_2$, $NiCl_2$, $FeCl_3$, $SbCl_4$, $ZnCl_2$, and $PtCl_4$ [1,2]. All of these halides catalyzed the decomposition of diazomethane; the reduction to the free metal occurred only with mercuric chloride. This had been previously found for silver salts [3]. However, it was shown [4] that α-haloalkyl-mercury compounds were formed by the reaction of diazomethane and phenyldiazomethane with the halogen salts of mercury; mercuric chloride was shown to react analogously with diazoacetic ester by Nesmeyanov and Povkh [5]. Attempts, by a series of investigators, to obtain organic derivatives of zinc [6], iron, tin [7], and phosphorus [8] by means of aliphatic diazo compounds ended in failure. Therefore, one could have concluded that the aliphatic diazo compounds, in contrast to the aromatic, cannot be used for the synthesis of various organo-elemental compounds, and the synthesis of organomercury compounds was a chance occurrence — an exception.

Since one of the authors had previously prepared aliphatic organoarsenic compounds by means of the diazo method [9], a detailed study was undertaken in order to determine the possibility of and establish the conditions for the synthesis of various organo-elemental compounds by the diazo method. The results of studies on the synthesis of organo-antimony, arsenic, and bismuth compounds are reported in this paper.

The methods for the synthesis of organoantimony compounds are very limited, and the number of known compounds of this series is small. Still smaller is the number of antimony alkyls containing substitutions in the radical. Only recently was the synthesis and properties of chlorovinyl antimony derivatives reported by Nesmeyanov and Borisov [10].

Organic and inorganic antimony chlorides are both very readily hydrolyzed so that experimentation with antimony derivatives is greatly complicated, especially, with aliphatic diazo compounds, which are so sensitive to the hydrogen halides. Nevertheless, it was possible to prepare chloromethyldichlorostibine and tri-(chloromethyl)-stibine from antimony trichloride and diazomethane, under the conditions given below, in satisfactory yields. The formation of chloromethyldichlorostibine from antimony trichloride and diazomethane (1:2) proceeds according to the scheme:

$$SbCl_3 + CH_2N_2 \longrightarrow ClCH_2SbCl_2 + N_2.$$

Tri-(chloromethyl)-stibine was obtained by the reaction of chloromethyldichlorostibine (1 mole) with excess diazomethane (3 moles):

$$ClCH_2SbCl_2 + 2CH_2N_2 \longrightarrow (ClCH_2)_3Sb + 2N_2.$$

Tri-(chloromethyl)-stibine, in contrast to other tertiary alkylstibines, is relatively stable in the air, but it slowly oxidizes and the substance clouds up as a result of the formation of the oxide. It does not react with water under the usual conditions, but on prolonged contact, (12-14 hours), the formation of a white precipitate occurs, apparently, as a result of hydrolysis and the formation of antimony oxides. The corresponding dibromide, which crystallizes readily in the form of red, shiny needles, is formed by the action of bromine on trichloromethyl antimony.

Di-(α-chloroethyl)-chlorostibine is readily formed by the reaction of trichlorostibine with diazoethane (1:2). This substance is somewhat more easily oxidized by atmospheric oxygen than trichloromethylstibine, but all are much more stable compounds when compared to the unsubstituted alkylstibines. Apparently, the presence of the chlorine atom in the α-position considerably decreases the tendency for the alkylstibines to be oxidized. This conclusion was supported by the fact that the formation of the acid was completed only after 15-20 hours when di-(α-chloroethyl)-chlorostibine was acted upon by hydrogen peroxide.

Antimony pentachloride does not form organoantimony compounds with diazomethane; the reduction of the pentavalent to the trivalent antimony takes place according to the reaction:

$$SbCl_5 + CH_2N_2 \longrightarrow SbCl_3 + CH_2Cl_2 + N_2.$$

Therefore, various α-haloalkyl derivatives of antimony can be obtained by means of the aliphatic diazo compounds in a manner analogous to that used to prepare the chloromethyl derivatives of arsenic [9]. It was thought to be of great interest to increase the amount of organic arsenic compounds synthesized by the diazomethane, to extend this method to other group V elements, as for example bismuth; the latter is reported below.

In contrast to diazomethane, diazoethane alkylates arsenic trichloride so readily that even if the ratio CH_3CHN_2: $AsCl_3$ = 1: 1.5 moles, only the formation of the secondary arsine takes place and almost no α-chloroethyldichloroarsine is formed. This shows that the rate of the reaction of the alkylation of α-chloroethyldichloroarsine is considerably greater than the rate of the reaction of arsenic trichloride and diazoethane. In contrast, the formation of tri-(α-chloroethyl)-arsine, obtained by the reaction of diazoethane and arsenic trichloride (4:1), or by the reaction of an excess of diazoethane with di-(α-chloroethyl)-chloroarsine:

$$AsCl_3 + nCH_3CHN_2 \longrightarrow (CH_3CHCl)_3As + nN_2$$
$$(CH_3CHCl)_2AsCl + CH_3CHN_2 \longrightarrow (CH_3CHCl)_3As + N_2,$$

occurs only with difficulty, so that the secondary arsine is always isolated with the tertiary arsine from the reaction products.

Tri-(A-chloroethyl)-arsine, a colorless oil, is an unstable substance which decomposes on storage, as well as upon distillation in not too great a vacuum.

A substance which contains very little hydrolyzable chlorine and separates from the reaction mixture as an amorphous powder not prone to crystallization is obtained from the reaction of bismuth trichloride with diazomethane either in ether or in benzene, although all the solvents are dried with sodium. This compound, according to analysis, closely corresponds to the oxide of chloromethyl bismuth, and is characterized by the following specific behavior: spontaneous combustion of this product in the air, spontaneous carbonization throughout the whole mass when touched with a hot glass rod. Apparently, the formation of the oxide occurs according to the scheme:

$$BiCl_3 \xrightarrow[-N_2]{+CH_2N_2} ClCH_2BiCl_2 \xrightarrow[-2HCl]{+H_2O} ClCH_2BiO.$$

A readily hydrolyzed, unstable chloride, which is not prone to recrystallization, is obtained by treating the oxide with hydrochlofic acid and evaporating the solution in vacuum. According to analysis, the substance resembles in structure chloromethyl dichlorobismuth.

Therefore, the reaction of aliphatic diazo compounds with antimony, arsenic, and bismuth halides can be looked upon as a new general method for the synthesis of organic compounds of these elements.

EXPERIMENTAL

In all of the experimental work reported below, the usual method was used to prepare the solutions of the diazo compounds from the corresponding alkylnitrosourea by the decomposition of the latter with a solution of potassium hydroxide in the presence of a solvent (ether, and thiophene-free benzene). The diazo compound, so obtained, was dried and then the amount of the diazo compound in the solution was determined by means of benzoic acid.

1. Preparation of chloromethyldichlorostibine. 26.2 g of CH_2N_2 in 1100 ml of benzene, dried over solid potassium hydroxide (3 hours) and over sodium ribbon (0.5 hour), was added to 57 g of $SbCl_3$ in 75 ml of absolute benzene. The apparatus, which consisted of a three-necked flask with a mercury-sealed stirrer, a dropping funnel, and a gas take off tube (leading to the atmosphere through a Tishchenko bottle with sulfuric acid), was swept with nitrogen before the experiment, while the flask was heated. Continuing the passage of the nitrogen, a solution of $SbCl_3$ in benzene was added to the warm apparatus, the mixture was cooled to +3 − +5°, and the solution of diazomethane added over a 45 minute period. The reaction was accompanied by the evolution of heat (cooling) and nitrogen. The mixture was left over night at room temperature. A small amount of a residue, hydrolysis products, gathered at the bottom of the flask. For distillation of the benzene, the reaction flask was connected with a distillation flask (50 ml) by means of a tube placed in the reaction

flask located some distance above the precipitate. The benzene solution was sucked over into the distillation flask in parts (there was a clamp on the tube connecting the flasks), where the benzene was continually distilled in vacuum (60 mm) in a stream of dry, oxygen-free nitrogen. (The pump had a trap, cooled to minus 15-20°, in the line from the apparatus).

The residue, after the distillation of the benzene – a dark oil, was vacuum distilled on a free flame without a condenser, and the distillate collected in another distilling flask from which it was fractionally distilled. There was a decomposition at the end of the distillation. 33 g of an oil, which crystallized on cooling, came over at 120-125° at 25 mm. The residue in the flask, a dark, brittle tar, consisted of metallic antimony.

In this way, crude chloromethylchlorostibine was obtained by fractionation, as a dense, colorless oil, the main part of which came over at 96-99° at 4 mm. The pure chloromethylchlorostibine was a colorless crystalline substance; needles, m.p. 36-38° (in a closed capillary); b.p. 86.5° at 2 mm, 91-98° at 7 mm, d_{20}^{20} 2.677. The molten substance remained fluid at room temperature for a long time; it only crystallized when cooled below 0°. It was easily hydrolized by water to form a white precipitate of antimony oxides. A dark precipitate was formed on boiling with aqueous alkali (reduced antimony oxides).

0.1884 g substance: 22.98 ml 0.1 N $AgNO_3$. 0.2257 g substance: 27.49 ml 0.1 N $AgNO_3$. 0.2031 g substance: 14.15 ml 1/6 N $KBrO_3$. 0.2374 g substance: 19.50 ml 1/6 N $KBrO_3$. Found %: Cl 43.25, 43.19; Sb 50.70, 50.24. $ClCH_2SbCl_2$. Calculated %: Cl 43.93; Sb 50.29.

2. Preparation of tri-(chloromethyl)-stibine. 21.9 g (1 mole) of chloromethylchlorostibine, in 30 ml of absolute benzene, was placed in the apparatus described and 12.4 g (3 moles) of CH_2N_2 in 510 ml of benzene (dried with sodium ribbon) was added at 5-6° (cooling). Upon the addition of about 2/3 of the diazomethane, an intense evolution of heat and nitrogen occurred. The mixture was left over night. The benzene was distilled, as in Experiment 1, from a 25 ml distillation flask. The residue after the distillation of the benzene (19.0 g), was an oily yellow colored liquid. The following fractions were obtained upon fractionation of the residue in a stream of nitrogen: 1) b.p. 86-101° at 3 mm –2.8 g; 2) b.p. 102-104° at 3 mm –4.1 g; 3) b.p. 104-106° at 3 mm –4.5 g.

Upon redistillation of the third and second fractions, tri-(chloromethyl)-stibine, b.p. 105° at 3 mm, was obtained in the form of a dense colorless oil (8 g); d_{20}^{20} 2.038.

The substance could be stored under water for a long time (12-14 hours), but all of it completely hydrolyzed forming a white residue. It clouded rapidly on the surface in the air, apparently, as a result of oxidation; in a thin layer, (on a glass) it rapidly changed into a white solid product.

0.3820 g substance: 41.11 ml 0.1 N $AgNO_3$. 0.1721 g substance: 18.86 ml 0.1 N $AgNO_3$. 5.068 ml substance: 2.600 mg CO_2; 1.294 mg H_2O. 5.630 mg substance: 2.875 mg CO_2; 1.300 mg H_2O. 0.2944 mg substance: 21.44 ml 1/6 N $KBrO_3$. 0.1976 mg substance: 14.36 ml 1/6 N $KBrO_3$. Found %: Sb 44.36, 44.26; C 13.99, 13.93; H 2.85, 2.58; Cl 38.16, 38.86 $(ClCH_2)_3Sb$. Calculated %: Sb 43.19; C 13.68; H 2.22; Cl 39.4.

3. Preparation of tri-(chloromethyl)-dibromostibine. 1 g of tri-(chloromethyl)stibine was dissolved in 3 ml of dry, redistilled carbon tetrachloride, and 0.6 g bromine in 2 ml of CCl_4 was added to the solution with hand shaking. The solution was filtered and the solvent was vacuum distilled. The residue – a white powder – was recrystallized from benzene: white shiny needles, m.p. 90-90.5° (shrinks at 89-90°).

0.1008 g substance: 4.66 ml 0.1 N $AgNO_3$. 0.4379 g substance: 6.39 ml 0.1 N $AgNO_3$. Found %: Br 36.95, 37.04 $(ClCH_2)_3SbBr_2$. Calculated %: Br 37.42.

4. Reaction of diazomethane with antimony pentachloride. 50 g of $SbCl_3$ in 55 ml of absolute benzene was treated with 4 g of diazomethane in 220 ml of benzene at minus 14-20° and, at the end, at –4 to –3°. The benzene was vacuum distilled. The residue – a violet colored oily liquid (21.5 g), which crystallized on standing – contained 8 g of trivalent antimony in contrast to the 12.2 g of pentavelent antimony used in the reaction, according to the analysis. On redistillation the residue came over at 99-100° (8 mm) as a liquid, which crystallized in the receiver and possessed all of the properties of antimony trichloride.

If the residue after distillation of the benzene was treated with hydrochloric acid (with heating), and the insoluble part extracted with benzene and dried with Na_2SO_4, then after the distillation of the solvent, a small amount of an oil, b.p. 250-270° and characteristic odor of diphenylmethane was obtained.

5. Preparation of di-(α-chloroethyl)-chloroantimony. The apparatus and the procedure was the same as for Experiment 1. A solution of 17.2 g of (1 mole) $SbCl_3$ in 50 ml of benzene was cooled to 0° and a solution of 8.44 g (2 moles) of CH_2N_2 in 485 ml of benzene, dried for 3 hours over KOH sticks and then for 0.5 hours over sodium ribbon, was added to it with stirring.

At first, the reaction was affected at 2-3° and, at the end, at 5-6° (cooling with ice and salt). The addition of the diazoethane required 1 hour. The mixture was left overnight. The benzene was distilled as in Experiment 1 (30 ml distillation flask). The residue was a brownish red oil (18 g). On distillation in vacuum, 10.5 g of di-(α-chloroethyl)-chloroantimony came over at 83-90° at 3 mm; a slightly colored, dense liquid.

Pure di-(α-chloroethyl)-chloroantimony was a colorless oil, b.p. 88-88.5° at 3 mm, or 69.5° at 1 mm, d_{20}^{20} 1.831. It clouded up on contact with air as a result of oxidation; it did not seem to hydrolyze in water.

8.035 mg substance: 4.963 mg CO_2; 1.988 mg H_2O. 7.305 mg substance: 4.240 mg CO_2; 1.510 mg H_2O. 12.68 mg substance: 6.374 ml 0.02 N $AgNO_3$. 15.02 mg substance; 7.637 ml 0.02 N $AgNO_3$. 0.305 g substance: 21.33 ml 1/6 N $KBrO_3$. 0.2360 g substance: 16.55 ml 1/6 N $KBrO_3$. Found %: C 16.84, 16.57; H 2.76, 2.31; Cl 36.52, 36.06; Sb 42.63 , 42.90. $(CH_3CHCl)_2SbCl$. Calculated %: C 16.9; H 2.82; Cl 37.5; Sb 42.84.

Dichlorodiethylchloroantimony (1.6 g), when oxidized with 5 ml of peroxide in 5 ml of water, slowly (15-20 hours) changed (mixing) into a white powder of dichloroethylstibianic acid (1.3 g), which did not melt when heated to 190°.

0.1716 g substance: 12.5 ml 1/6 N $KBrO_3$. 0.2900 g substance: 20.9 ml 1/6 N $KBrO_3$. 13.59 g substance: 4.656 ml 0.02 N $AgNO_3$. 12.12 g substance: 4.17 ml 0.02 N $AgNO_3$. Found %: Sb 44.55, 44.08; Cl 24.30, 24.40. $(CH_3CHCl)_2SbO_2H$. Calculated %: Sb 43.30; Cl 25.24.

6. Preparation of di-(α-chloroethyl)-chloroarsine. A solution of 13.8 g of diazoethane (2.5 moles) in 500 ml of benzene, dried over KOH sticks for 3 hours, was added dropwise (about 1 hour) to a solution of 17 g (1 mole) of redistilled $AsCl_3$ in 50 ml of dry benzene. The reaction was effected at first at 0°, and, at the end, at 3-5° (cooling with ice and salt). The mixture was left over night and then the benzene was distilled off at 50-100 mm. The residue, a colored oil, was vacuum distilled, di-(α-chloroethyl)-chloroarsine, came over at 51-54° at 1 mm; yield 12 g (40% of theory on the diazoethane).

With a ratio of $AsCl_3$ to diazoethane of 1:1.5 moles, on distillation, the excess $AsCl_3$ first came over and then di-(α-chloroethyl)-chloroarsine, in a somewhat greater yield than above, distilled. When the amount of the diazoethane was greater than 2.5 moles to 1 mole of $AsCl_3$, some of the tertiary arsine was formed along with the secondary derivative. The preparation of the former is given below.

Di-(α-chloroethyl)-chloroarsine was a colorless oil, b.p. 51.5° at 1 mm, 61-61.5° at 3 mm, d_{20}^{20} 1.553, $n_D^{21.5}$ 1.5370. It darkened on standing.

3.850 mg substance: 2.835 mg CO_2; 1.035 mg H_2O. 4.920 mg substance: 8.700 mg CO_2; 1.885 mg H_2O. 11.71 mg substance: 7.369 ml 0.02 N $AgNO_3$. 12.82 mg substance 8.07 ml 0.02 N $AgNO_3$. 0.1172 g substance: 9.8 ml 0.1 N I_2. 0.1528 g substance: 12.7 ml 0.1 N I_2. Found %: C 20.08, 20.51; H 3.79, 4.19; Cl 44.63, 44.65; As 31.71, 31.60. $(CH_3CHCl)_2AsCl$. Calculated %: C 20.23; H 3.37; Cl 44.88; As 31.49.

7. Preparation of tri-(α-chloroethyl)-arsine. 19 g of redistilled $AsCl_3$ (1 mole) was treated in the above manner with 23.2 g of diazoethane (4 moles) in 950 ml of benzene. The reaction mixture, containing an excess of diazoethane, was left in an ice bath overnight. The further processing was the same as Experiment 6. The residue was fractionated in vacuum and a fraction, b.p. 40-68° at 1 mm, 7.9 g; and a fraction b.p. 69.5-70.2° at 1 mm, 7.2 g, were obtained. The last fraction was pure tri-(α-chloroethyl)-arsine. On redistillation in a smaller vacuum, it decomposed considerably: b.p. 81-82° at 2 mm, 94-95° at 4 mm. Pure tri-(α-chloroethyl)-arsine was a colorless oil, d_{20}^{20} 1.445, n_D^{25} 1.5307; on storage under ordinary conditions, it slowly darkened; depending on the length of time stored it gave, in addition to tri-(α-chloroethyl)-arsine, a lower-boiling fraction and considerable tarry residue on distillation.

4.455 mg substance: 4.465 mg CO_2; 1.975 mg H_2O. 4.595 mg substance ; 4.635 mg CO_2; 1.940 mg H_2O. 0.2283 g substance: 25.80 ml 0.1 N AgNO. 0.1391 g substance: 15.65 ml 0.1 N $AgNO_3$. 0.1656 g substance: 12.59 ml 0.1 N $Na_2S_2O_3$. 0.2123 g substance: 15.99 ml 0.1 N $Na_2S_2O_3$. Found %: C 27.40, 27.51; H 4.97, 4.72; Cl 40.07, 39.90; As 28.52, 28.25. $(CH_3CHCl)_3As$. Calculated %: C 27.17, H 4.53; Cl 40.0; As 28.26.

Di-(α-chloroethyl)-chloroarsine was obtained on the redistillation of the fraction, with b.p. 40-68° at 1 mm, and was identified by its boiling point, refractive index, and analysis for arsenic.

Tri-(α-chloroethane)-arsine can also be obtained by the action of diazoethane (1.5 mole) on di-(α-chloroethyl)-chloroarsine (1 mole) under the conditions given above. But under these conditions, the reaction products contained some unalkylated di-(α-chloroethyl)-chloroarsine along with the tri-α-chloroethyl)-arsine.

8. Reaction of diazomethane with bismuth trichloride. A solution of 5 g of $BiCl_3$ in 70 ml of absolute ether was prepared in a separate dish isolated from the air, and, while it was carefully protected from moisture, was added to the reaction flask under nitrogen. The reaction flask, fitted with a mercury-sealed stirrer, a dropping funnel, a thermometer, and a gas outlet tube, was dried carefully before the experiment by blowing dry nitrogen through while it was heated. 1.2 g of diazomethane in ether (70 ml) dried over sodium was added, dropwise with stirring and cooling (0-3°), in 40 minutes. With this, a violent evolution of nitrogen and the formation of a light yellow, almost colorless, precipitate occurred in the flask. The liquid was allowed to stand overnight at the temperature of melting ice. The precipitate was filtered by sucking over the reaction mixture, containing the suspended precipitate (mechanical stirrer) onto a hermetically sealed funnel by means of a vacuum. The precipitate and the funnel were placed in a vacuum desiccator. After removal of the ether, a light, silver green powder was obtained as the reaction product. Yield ~5 g. The substance dissolved in concentrated hydrochloric acid. When it was touched with a heated stick, a spontaneous carbonization occurred throughout the entire mass of the powder. •

4.00 mg substance: 0.785 mg CO_2; 0.540 mg H_2O. 3.375 mg substance: 0.605 mg CO_2; 0.795 mg H_2O. 0.1428 g substance: 0.1058 g Bi. 15.91 mg substance: 2.27 ml 0.02 N $AgNO_3$. 11.19 mg substance: 1.52 ml 0.2 N $AgNO_3$. Found %: C 5.35, 4.89; H 1.9, 2.63; Cl 9.63, 10.12; Bi 74.0. CH_2ClBiO. Calculated %: C 4.42; H 0.73; Cl 13.0; Bi 76.2.

1.5 g of the substance, whose analysis is given above, was dissolved in 3 ml of concentrated hydrochloric acid and the solution was evaporated in vacuum (2-3 mm) at 40°. The residue was a light yellow syrupy mass which crystallized after some time.

7.705 mg substance: 1.165 mg CO_2; 1.30 mg H_2O. 7.925 mg substance: 1.255 mg CO_2; 1.405 mg H_2O. 0.1217 g substance: 0.0687 g Bi. 0.1161 g substance: 10.31 ml 0.1 N $AgNO_3$. Found %: C 4.12, 4.31; H 1.89, 2.05; Bi 56.7; Cl 31.48. $CH_2ClBiCl_2$. Calculated %: C 3.65; H 0.608; Bi 63.47; Cl 32.42.

The substance obtained decomposed during the purification. When it was dissolved in absolute solvents prepared in the usual manner, a precipitate, apparently oxides, formed.

SUMMARY

1. It was shown that the diazo method for the synthesis of aliphatic organo-elemental compounds can be applied for the preparation of organo-antimony, arsenic, and bismuth compounds.

2. Chloromethyldichlorostibine and tri-(chloromethyl)-stibine were obtained by the reaction of antimony trichloride with diazomethane; and di(α-chloroethyl)stibine with diazoethane. Antimony pentachloride reacted with a molar quantity of diazomethane to form antimony trichloride.

3. Di-(α-chloroethyl)-chloroarsine and tri-(α-chloroethyl)-arsine could be obtained by the reaction of arsenic trichloride with diazoethane. The latter substance was an unstable compound, which decomposed when stored under ordinary conditions.

4. Bismuth trichloride and diazomethane formed the unstable oxide of chloromethyl bismuth, which, on treatment with hydrochloric acid, gave the unstable chloromethyldichlorobismuth.

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SYNTHESIS OF ALIPHATIC ORGANO-ELEMENTAL COMPOUNDS BY THE DIAZO METHOD

II. SYNTHESIS OF COMPOUNDS OF THE GROUP V ELEMENTS – ORGANO-PHOSPHORUS COMPOUNDS

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In the previous communication [1], it was shown that aliphatic diazo compounds can be used for the synthesis of organo-antimony, arsenic, and bismuth compounds. In order to increase the scope of this reaction, the synthesis of organophosphorus compounds by the diazo method was studied; with the expectation of producing the difficultly accessible, and little investigated halodialkylphosphine compounds.

In 1947 Plets [2] reported that the reaction of diazomethane with phosphorus trichloride leads to the formation of tarlike products from which no homogeneous compound could be isolated. Previously, Staudinger also could not observe any organophosphorus compound formation upon the reaction of PCl_3 with diazomethane [3]. Therefore, in contrast to the aromatic diazo compounds [4], the aliphatic had not been used up to now for the preparation of organophosphorus compounds. However, it was shown by the authors that under favorable conditions,(low temperatures) aliphatic diazo compounds could be used successfully for the preparation of α-halodialkylphosphine compounds. In principle this reaction differs little from the previously studied reaction of the aliphatic diazo compounds with the halides of other elements.

At room temperature, diazomethane and diazoethane react very violently with phosphorus trichloride (in ether solution) to form nitrogen and a tarlike precipitate, which liquifies in the air. However, when the reaction temperature is decreased to minus 60-50°, the amount of precipitate is greatly decreased, and chloromethyldichlorophosphine and α-chloroethyldichlorophosphine (respectively) are obtained as the main reaction products in 40% yields calculated on the diazo compound.

$$PCl_3 \xrightarrow{CH_2N_2} ClCH_2PCl_2 + N_2$$

$$PCl_3 \xrightarrow{CH_3CHN_2} CH_3CHClPCl_2 + N_2$$

Small amount of esters of dichlorophosphoric acid (CH_3OPCl_2 and $C_2H_5OPCl_2$ respectively) are obtained as side products, as a result of the alkylation of dichlorophosphoric acid due to the partial hydrolysis of PCl_3 with traces of water introduced with the solvents.

$$PCl_3 + H_2O \longrightarrow HOPCl_2 + HCl; \qquad RCHN_2 + HOPCl_2 \longrightarrow RCH_2OPCl_2 + N_2.$$

On the reaction of phosphorus trichloride with diazobutane, α-chloro-n-butyldichlorophosphine is formed (in addition to the side product, butyl dichlorophosphite) which, in further processing is transformed into the acid chloride of α-chloro-n-butylphosphinic acid, which was isolated from the reaction products.

The ease of oxidation of the alkyldichlorophosphines to form derivatives of P^V was also observed for α-chloroethyldichlorophosphine (cotton soaked with $CH_3CHClPCl_2$ flamed spontaneously in the air), while chloromethyl- and bromomethyldihalophosphines are relatively stable in the air.

Phosphorus tribromide reacts analogously with diazomethane to give 50% yield of bromomethyldibromophosphine. A series of its derivatives was also prepared (see the experimental section). It is interesting that chloromethyl phosphorus tetrachloride is readily chlorinated to CCl_3PCl_4, which forms the stable polychloroacid chloride $CCl_3PO(Cl)OH$, m.p. 79°, on hydrolysis with water. Trichloromethylphosphinic acid can be obtained by the hydrolysis of the above acid, as well as from diethyl trichloromethylphosphinate; reported by Kamay [5], with hydrochloric acid (in a sealed ampoule); m.p. 87-89°.

The reaction of α-chloroalkyldichlorophosphines with aliphatic diazo compounds does not lead to the formation of di- and trichloroalkylphosphines; the reaction, instead results in more complex solid products. Analogous compounds are obtained as side products from the reaction of aliphatic diazo compounds with PCl_3 and PBr_3.

Therefore, the above reaction can be used as a convenient method for the synthesis of the difficultly accessible primary alkylhalophosphines. However, di- and trialkyl-substituted derivatives of phosphorus, as well as the mono- can be prepared with the aid of aliphatic diazo compounds, if the phosphorus pentahalides are used. These reactions were studied with diazomethane and diazoethane, and phosphorus pentachloride. It appears that the course of this reaction was effected by the lower solubility of PCl_5 in organic solvents, as compared with the solubility of the alkyl substituted derivatives of PCl_5($RPCl_4$, R_2PCl_3, etc), and by the greater rate of alkylation of the latter, when compared to PCl_5.

The reaction, for example, of diazomethane with phosphorus pentachloride, apparently, proceeds under the conditions of "excess" diazo-compound and does not stop at the monoalkylated stage, but goes on to the trialkylated, so that the oxide of tri-(chloromethyl)-phosphine forms in a 50-70% yield according to the equation:

$$PCl_5 + 3CH_2N_2 \longrightarrow (ClCH_2)_3PCl_2 \xrightarrow[\text{or } SO_2]{\text{moisture-}} (ClCH_2)_3PO.$$

The reaction between diazoethane and phosphorus is more complex; the acid chloride of di-(α-chloroethyl)-phosphinic acid, which gave di-(α-chloroethyl)-phosphinic acid on hydrolysis, was isolated from the reaction products.

It is interesting that phosphorus oxychloride and oxybromide, in contrast to phosphorus pentachloride, could not be alkylated with diazomethane or diazoethane even on the artificial decomposition of the diazo compounds with catalysts (Cu, $CuSO_4$). The only product of the reaction, for example with $POCl_3$, along with the recovered phosphorus oxychloride, was the ester of dichlorophosphoric acid formed in small quantities as a result of the partial hydrolysis of phosphorus oxychloride followed by the alkylation of the dichlorophosphoric acid with the diazo compound.

$$POCl_3 \xrightarrow{H_2O} HOPOCl_2 \xrightarrow{CH_2N_2} CH_3OPOCl_2.$$

EXPERIMENTAL

1. Chloromethyldichlorophosphine, $ClCH_2PCl_2$. An ether solution (1 mole) of diazomethane (25 g of CH_2N_2 in 750 ml ether), dried by a three hour cooling to −70° over solid potassium hydroxide, was added with efficient mechanical stirring to a solution of 200 g of PCl_3 (2 5 mole) in 200 ml of dry ether cooled to −70°. The temperature of the reaction mixture was kept at minus 55-65°. An energetic reaction occurred, accompanied by the evolution of nitrogen (about 14 liters of gas) and the formation of a white precipitate. The mixture was then allowed to stand overnight, slowly warming up to room temperature; then the reaction products of five experiments were combined and processed together. The precipitate was filtered onto a glass filter protected from moisture, and washed many times with dry ether; it was dried in a vacuum desiccator, over P_2O_5 and solid alkali to remove the ether. A total of 32 g of dry residue, which hydrolyzed in the air, was obtained.

The residue − organophosphorus compounds − was soluble in water, alcohols, ketones, and insoluble in benzene and chloroform. The substance was decomposed on recrystallization.

The ether of the filtrate was distilled through a column and the residue fractionated through the column, first at ordinary pressure and then at 140 mm. Besides PCl_3, the following fractions were collected (uncorrected b.p.'s): I) 42-47.5° −13 g; II) 47-62° at 140 mm, −54 g; III) 62-76° at 140 mm −7 g; IV) 77-78° at 140 mm −175 g.

Fraction I was redistilled at ordinary pressure: a) 84-90° −3.0 g; b) 91-92° −4.8 g; c) 92-93.5°−3 g.. Fraction IB had b.p. 91-92° (uncorrected); or 94-95° (corrected).

d_{20}^{20} 1.3995; n_D^{20} 1.4750.

Found %: Cl 52.91, 53.10. CH_3OPCl_2. Calculated %: Cl 53.38.

Therefore, fraction IB was methyl dichlorophosphate described by Kovalevsky [7]; b.p. 95-96°; d_4^{20} 1.3980; n_D^{20} 1.47725.

Fraction II was redistilled at ordinary pressure_ d) 102.3-105° (uncorrected) −16.2 g; e) 105-107° (uncorrected) −31.3 g; f) a small amount of a higher boiling fraction. Fraction IIe had b.p. 105-107.6° (uncorrected) or 108-110° (corrected; the substance did not contain P^{III}).

Found %: Cl 68.38, 69.36. $POCl_3$. Calculated %: Cl 69.38. Therefore Fraction IIe was phosphorus oxychloride•.

Fraction IV, b.p. 77-78° (uncorrected) or 80-81° (corrected); d_{20}^{20} 1.5289, n_D^{20} 1.5247 – was a dense, transparent, colorless liquid with a sharp, unpleasant odor. The substance clouded in the air as a result of hydrolysis.

2.860 mg, 5.410 mg substance: 0.845 mg, 1.0670 mg CO_2; 0.475 mg, 0.800 mg H_2O. 9.905 mg, 12.160 mg substance: 9.719 ml, 12.160 ml 0.02 N $AgNO_3$. 0.2045 g, 0.2542 g substance in 25 ml 0.5 N KOH: 27.30 ml, 27.4 ml 0.1 N $AgNO_3$. 0.3136 g, 0.3304 g substance: 0.3955 g, 0.4155 g molybdate. 0.3945 g substance; 16 g benzene: Δt 0.830°. Found %: C 8.05, 7.31; H 1.46, 1.46; total Cl 69.59, 69.43; hydrolyzable Cl 47.31, 47.08; P 20.85, 20.81; M 152. $ClCH_2PCl_2$. Calculated %: C 7.90; H 1.32; total Cl 70.25; hydrolyzable Cl 46.84; P 20.45; M 151.5.

Therefore Fraction IV was chloromethyldichlorophosphine (yield 40% of the theoretical on the diazomethane).

2. Phosphorus chloromethyltetrachloride, $ClCH_2PCl_4$. 2.5 g of chlorine (1 mole) in 10 ml of CCl_4 was added at 0 to +5° to a solution of 5 g (1 mole) of chloromethyldichlorophosphine in 5 ml CCl_4. A white crystalline precipitate formed rapidly, while the color of the chlorine disappeared. Then about 80% of the solvent was vacuum distilled at not over 30-35° (in the bath). The residue (5.5 g) was filtered and washed with cold CCl_4 (all of the operations were performed in the absence of moisture). The white crystals fumed in the atmosphere and liquified; m.p. 102-104° (decomp.) in a closed capillary.

A partial decomposition of the substance occurred on recrystallization.

0.1090 g substance in 25 ml 0.5 N KOH in the cold: 19.85 ml 0.1 N $AgNO_3$. Found %: hydrolyzable Cl 64.64. $ClCH_2Cl_4$. Calculated %: hydrolyzable Cl 64.39.

3. The di-acid chloride of chloromethyl phosphinic acid, $ClCH_2POCl_2$. a) The oxidation of chloromethylchlorophosphine with nitrogen dioxide. 10 g of chloromethylchlorophosphine, in 10 ml of dry CCl_4, was oxidized at −5 to 0° with dry nitrogen dioxide, which was slowly passed into the reaction mixture (3.7 g of NO_2 in 30 min). The nitrogen dioxide was added as rapidly as it was decolorized. Oxidation stopped just as soon as a permanent red color formed, due to the formation of tarry products. The reaction mixture was then swept with dry air and immediately vacuum distilled. 7 g (yield 60% of the theoretical) of the di-acid chloride of chloromethylphosphinic acid, b.p. 103° at 30 mm, was obtained; it was a colorless, dense liquid, with a characteristic acid chloride odor.

d_{20}^{20} 1.6444; n_D^{20} 1.4945.

11.800 mg substance: 10.55 ml 0.02 N $AgNO_3$. 0.1410 g substance in 25 ml 0.5 N KOH: 16.9 ml 0.1 N $AgNO_3$. 0.2756 g substance: 16 g benzene: Δt 0.515°.

Found %: total Cl 63.48; Hydrolyzable Cl 42.54; M 171. CH_3OCl_3P. Calculated %: Total Cl 63.58; Hydrolyzable Cl 42.38; M 167.5.

b) The treatment of phosphorus chloromethyltetrachloride with sulfur dioxide. Phosphorus chloromethyltetrachloride, obtained in the above way from 10 g of chloromethyldichlorophosphine, was treated in the cold (without any preliminary distillation of the solvent) with dry sulfur dioxide until the precipitate dissolved, and subsequently for 15 minutes. The CCl_4 is removed in vacuum at 30-35° (in a bath) and the residue fractionated. 8.5 g of a liquid which was $ClCH_2POCl_2$, b.p. 102-103° at 30 mm or 63° at 2 mm, was obtained. Yield about 80% of the theoretical.

Found %: Hydrolyzable Cl 42.03. $ClCH_2POCl_2$. Calculated %: Hydrolyzable Cl 42.38.

4. Chloromethylphosphinic acid, $ClCH_2PO(OH)_2$. 2 g of the diacid chloride of chloromethylphosphinic acid was added, in parts, to 10 ml of water; it dissolved with the evolution of heat. After standing in a vacuum desiccator over P_2O_5 for one week, it crystallized. The wet crystals of the chloromethyl phosphinic acid were pressed on a plate and recrystallized from a mixture of benzene and nitromethane: thin long needles, m.p. 92°. Yield – quantitative.

• Careful distillation of the initial PCl_3 in the same column (20 theoretical plates) resulted in the isolation of the corresponding quantity of $POCl_3$. Therefore, the oxychloride was introduced as an impurity in the phosphorus trichloride.

5.862 mg, 4.230 mg substance: 2.010 mg, 1.428 mg CO_2; 1.715 mg, 1.428 mg H_2O. 15.10 mg, 15.11 mg substance: 5.630 ml, 5.700 ml 0.02 N $AgNO_3$. Found %: C 9.35, 9.21; H 3.27, 3.25: Cl 26.47, 26.80. Calculated %: C 9.19; H 3.07; Cl 27.20.

The substance was hygroscopic; the silver salt dissolved readily in water. Methyl chloride was not formed on heating with alkali.

5. Aniline salt of chloromethylphosphinic acid, $ClCH_2PO(OH)_2 \cdot C_6H_5NH_2$. 0.5 g of the acid was mixed with benzene with an excess of aniline (2 ml). After standing for two days, the precipitate was filtered and recrystallized from alcohol. Thin needles, m.p. 183°, (with decomp.) Yield – quantitative.

4.790 mg, 3.950 mg substance: 0.3008 ml, 0.2450 ml N_2 (20°, 752 mm) 0.1337 g substance: 12.0 ml 0.1 N KOH (phenolphthalien). Found %: N 7.17, 7.08; equiv. 111. Calculated %: N 6.26; equiv. 111.7.

6. Ethyl ester of chloromethylphosphinic acid, $ClCH_2PO(OC_2H_5)_2$. An alcoholic solution of sodium ethylate (2.8 g of sodium in 55 ml of absolute alcohol) was added to 8.3 g of the di-acid chloride of chloromethylphosphinic acid in 10 ml of ether at 0-5° until neutral to Congo. After filtration of the sodium chloride precipitate and distillation of the alcohol and the ether, the residue was fractionated in vacuum. Ethyl chloromethylphosphinate was a colorless liquid with a fruity odor; b.p. 86-87° at 2.5 mm.

d_{20}^{20} 1.1909; n_D^{20} 1.4360.

4.185 mg, 3.985 mg substance: 4.840 mg, 4.610 mg CO_2; 2.305 mg, 2.205 mg H_2O. 12.380 mg substance: 18.84 ml 0.02 N $AgNO_3$. 0.2552 g substance; 16 g benzene: Δt 0.435°. Found %: C 31.54, 31.55; H 6.16, 6.19; Cl 18.84; M 187.5. $ClCH_2PO(OC_2H_5)_2$. Calculated %: C 31.17; H 6.43; Cl 19.03; M 186.5.

7. α-Chloroethyldichlorophosphine, $CH_3CHClPCl_2$. 30 g of diazoethane (1 mole) in 800 ml of dry ether, dried in the usual manner, was added dropwise to 190 g of PCl_3 (2.5 mole) in 200 ml of dry ether cooled to –70°. The reaction was run at minus 55-60° in a nitrogen atmosphere; a considerable amount of heat evolved and a clouding of the solution occurred (white precipitate). The mixture was allowed to come to room temperature overnight and the precipitate dissolved completely. The ether was removed from the reaction products of 4 experiments (through a column) and the residue was distilled through a column. In addition to PCl_3 the following fractions were collected: I) to 44° (100 mm) –5 g; II) 40-46° (100 mm) –52 g; III) 46.5-50.9° (100 mm) –7 g; IV) 51.0 –52° (100 mm) –22 g; V) 53-61° (50 mm) –5 g; VI) 61.5-62.5° (50 mm) –100 g; VII) higher boiling residue – to 70° (7 mm) –10 g.

Fraction II was redistilled at ordinary pressure. The bulk of it distilled at 107-109° (corrected). The fraction did not contain trivalent phosphorus.

Found %: Cl 68.3, 69.1. $POCl_3$. Calculated %: Cl 69.38.

Therefore, Fraction II was phosphorus oxychloride (see Experiment 1).

The substance in Fraction IV, b.p. 51.0-52° at 100 mm and 117-118° (with decomp.) at ordinary pressure:

d_{20}^{20} 1.3300; n_D^{20} 1.4640.

Found %: total Cl 51.30, 51.80; hydrolyzable Cl 50.85, 51.48. P total 20.76; P^{III} 19.80; M 157, 150. $C_2H_5OPCl_2$. Calculated %: Cl hydrolyzable 48.30; P^{III} 21.1; M 147.

Therefore, Fraction IV was impure ethyl dichlorophosphate. Literature data [7]: b.p. 117-118°, d^0 1.316, n_D^{22} 1.7776.

For identification, the preparation was treated with a mixture of alcohol and diethylaniline. 5.3 g of Fraction IV was added to 15 g of diethylaniline, 5 g of absolute alcohol, and 50 ml of ether with cooling; the mixture was left over night. Diethylaniline hydrochloride (12 g) was filtered off and the filtrate was twice distilled in vacuum. 7 g of triethyl phosphate, b.p. 49° at 12 mm and n_D^{20} 1.4130 was obtained; this corresponded to the results given in the literature.

Fraction VI, b.p. 61.5-62.5° (uncorrected) at 50 mm or 63.5-64.5° (corrected) at 50 mm, was a colorless substance which fumed in the air. Cotton soaked with this substance flamed in the air.

d_{20}^{20} 1.4232; n_D^{20} 1.5090.

5.290 mg substance: 2.720 mg CO_2; 1.215 mg H_2O; 11.52 mg substance: 10.53 ml 0.02 N $AgNO_3$. 0.1870 g substance; 16 g benzene. Δt 0.355°. 0.1857 g, 0.1470 g substance. In 25 ml water (it hydrolyzed within 25 min). 22.50 ml 17.8 ml 0.1 N $AgNO_3$. Found %: C 14.10; H 2.55; Hydrolyzable Cl

43.02, 42.97; Total Cl 64.81; M 167.5. $CH_3CHClPCl_2$. Calculated %: C 14.51; H 2.41; Hydrolyzable Cl 42.90; Total Cl 64.35; M 165.5.

Therefore, Fraction VI was α-chloroethyldichlorophosphine (yield 35 % of theoretical based on the diazoethane).

8. Phosphorus α-chloroethyltetrachloride – $CH_3CHClPCl_4$. 5 g of α-chloroethyldichlorophosphine in 5 ml of CCl_4 was chlorinated at -5 to 0° with the calculated amount of chlorine in CCl_4. A white precipitate formed which, after removal of the main part of solvent, was filtered and washed with cold CCl_4. Fine, hygroscopic crystals were obtained.

0.1237 g substance. saponified in 25 ml 0.5 N. KOH, 20.75 ml 0.1 N. $AgNO_3$. Found %: hydrolyzable Cl 59.55. $CH_3CHClPCl_4$. Calculated %: hydrolyzable Cl 60.04.

9. Di-acid chloride of α-chloroethylphosphinic acid – $CH_3CHClPOCl_2$. A solution of 7.5 g of chlorine (1.05 mole) in 50 ml of CCl_4 was added dropwise, with cooling with ice and salt, to a solution of 16.5 g of $CH_3CHClPCl_2$ in 15 ml of CCl_4. The precipitated tetrachloride was treated, without separation, with a stream of SO_2 until it dissolved and then for 10 minutes more. Then the solvent was removed (half at ordinary pressure and the rest in vacuum). The residue was distilled; everything distilled at 70° at 8 mm. Yield – 90-95 % of theory. It was a colorless liquid with a characteristic acid chloride odor.

d_{20}^{20} 1.5424; n_D^{20} 1.4930.

0.1423 g substance. saponified in 25 ml 0.5 N. KOH; 15.5 ml 0.1 N. $AgNO_3$. 11.30 mg, 11.50 mg substance: 9.396 ml, 9.609 ml 0.02 N. $AgNO_3$. 4.974 mg, 4.894 mg substance: 2.428 mg, 2.372 mg CO_2; 1.199 mg, 1.1210 mg H_2O. 0.2174 g substance; 16 g benzene: Δt 0.393°. Found %: C 13.34, 13.31; H 2.70, 2.70; hydrolyzable Cl 38.62; Total Cl 58.94, 59.26; M 178; $CH_3CHClPOCl_2$. Calculated %: C 13.23; H 2.20; hydrolyzable Cl 39.10; Total Cl 58.68. M 181.5.

10. α-Chloroethylphosphinic acid – $CH_3CHClPO(OH)_2$. 2g of $CH_3CHClPOCl_2$ was hydrolyzed with 3 ml of water. The excess water was removed in a desiccator over P_2O_5. The crystalline mixture was pressed on a plate, and the crystals recrystallized from a mixture of benzene and nitromethane.

Colorless needles; M.p. 99-100°. Yield – quantitative.

3.494 mg, 4.395 mg substance: 2.205 mg, 2.750 mg CO_2; 1.297 mg, 1.507 mg H_2O. 10.70 mg, 14.20 mg substance: 3.73 ml, 4.98 ml 0.02 N. $AgNO_3$. . Found %: C 17.21. 17.07; H 4.15. 3.83; Cl 24.75, 24.90. $CH_3CClPO(OH)_2$. Calculated %: C 16.61; H 4.25; Cl 24.57.
The silver salt was readily soluble in water.

11. Anilide of α-chloroethylphosphinic acid – $CH_3CHClPO(NHC_6H_5)_2$. An excess of aniline (5 g) was added to 2 g of the diacid chloride in benzene. After 24 hours the aniline hydrochloride was filtered off; it was washed with acidified water to remove the excess aniline, and the benzene was removed in vacuum from the dried solution. The noncrystalline oil was dissolved in alcohol; the addition of water precipitated white crystals. The m.p. was 154-155° after recrystallization from aqueous alcohol.

11.50 mg; 10.98 mg substance: 4.00 ml, 3.74 ml 0.02 N. $AgNO_3$. 3.300 mg, 4.930 mg substance: 0.30184 ml, 0.45864 ml N_2 (27°, 745 mm). Found %: Cl 12.33, 12.20; N 10.15, 10.35. $CH_3CHClPO(NHC_6H_5)_2$. Calculated %: Cl 12.05, N 9.56.

12. Ethyl ester of α-chloroethylphosphinic acid – $CH_3CHClPO(OC_2H_5)_2$. 50 ml of dry ether, 3 g of absolute alcohol and 9 g of diethylaniline were placed in a flask. A solution of 5.4 g of the di-acid chloride of α-chloroethylphosphinic acid in 10 ml of ether was added, dropwise in the cold (ice and salt). After 24 hours the diethylaniline hydrochloride was filtered; the excess diethylaniline was removed with acidified water, the ether layer dried, and the ether removed.

On distillation, a fraction, b.p. 93° at 5 mm or 96° at 7 mm, was collected. The yield of the ester – 3.5 g. It was a colorless liquid with a pleasant fruity odor.

d_{20}^{20} 1.1474; n_D^{20} 1.4370.

17.200 mg, 26.010 mg substance: 4.25 ml, 6.50 ml 0.02 N. $AgNO_3$. 0.2177 g substance; 16 g benzene: Δt 0.360°. Found %: Cl 17.54, 17.74; M 193. $CH_3CHClPO(OC_2H_5)_2$. Calculated %: Cl 17.71; M 200.5.

13. Reaction of diazobutane with phosphorus trichloride. a) Preparation of nitrosobutylurea. Hydrochloric acid was added dropwise with cooling to -5to 0° to a solution of 100 g of butylamine in 300 ml of water until an acidic reaction to methyl red was obtained. 400 g of water and 250 g of urea were added to the solution, and it was refluxed for three hours. After cooling, 120 g of sodium nitrite in 300 g of water was added to the reaction mixture (the main part of the crystals of the butyl urea dissolved), and the mixture slowly added to a mixture of 95 g of sulfonic acid and 600 g of finely chopped ice with energetic stirring and cooling to -5 to +5°.

The nitroso butylurea separated as a light foam, which was filtered on a glass filter, washed with a small amount of water, and dried in a desiccator. It was stored at temperatures below 10°.

b) Preparation of diazobutane. 100 g of nitrosobutylurea, was added, in portions with shaking and cooling to -5 – 0°, to a mixture of 500 ml of urea and 200 ml 70% aqueous solution of KOH. The ether layer was slowly colored red-orange. In order to prevent the decomposition of the nitrosomethyl urea, the ether layer containing the diazobutane was decanted. The yield was 25 g of diazobutane (analyzed with benzoic acid).

c) Preparation of the acid chloride of α-chlorobutylphosphinic acid – $CH_3(CH_2)_2CHClPOCl_2$. 22 g of diazobutane (1 mole) in 450 ml of ether, dried in the usual manner by cooling over KOH, was added dropwise with cooling, by means of CO_2 and acetone, to a solution of 70 g (2 moles) of PCl_3 in 100 ml of dry ether. The reaction occurred rapidly. After addition of the diazo compound, the ether was distilled through a column, and the residue fractionated. The following fractions were collected: I) b.p. 63-64.5° at 30 mm – 7 g, II) b.p. 84° at 25 mm – 10.5 g.

Fraction I boiled, at ordinary pressure, at 155-157° with decomposition.

d_4^{20} 1.1661.

Found %: Hydrolyzable Cl 40.0; Total Cl 39.4; P^{III} 17.7; M 180. $C_4H_9OPCl_2$. Calculated %: Hydrolyzable Cl 40.5; Total Cl 40.5; P^{III} 17.7; M 175.

Therefore, Fraction I was the acid chloride of butylphosphoric acid, whose constants were reported by Kovalevsky [7]: b.p. 157°, d_4^{20} 1.1657.

Fraction II, b.p. 84° at 25 mm, was a colorless liquid with a sharp acid chloride odor. The product did not contain P^{III}.

d_{20}^{20} 1.3236; n_D^{20} 1.5010.

0.1067 g, 0.1080 g substance in 25 ml 0.5 N KOH: 10.30 ml, 10.60 ml 0.1 N $AgNO_3$. 10.605 mg substance: 7.585 ml 0.02 N $AgNO_3$. 0.2300 g substance; 16 g benzene: Δt 0.330°. Found %: Hydrolyzable Cl 34.9; Total Cl 50.75; M 212. Calculated %: hydrolyzable Cl 33.89; Total Cl 50.84; M 209.5.

Therefore, this fraction was the acid chloride of α-chlorobutylphosphinic acid.

14. Reaction of diazomethane and PBr_3. Bromomethyldibromophosphine – $BrCH_2PBr_2$. A solution of 2.72 g of diazomethane (1 mole) in 150 ml of ether, dried in the usual manner by cooling over solid KOH and then for 2 hours over sodium ribbon, was added, slowly, with stirring at a temperature of minus 50-55°, to a solution of 52.7 g (3 moles) of PBr_3 in 50 ml of ether.

The diazomethane decomposed as it was added, and a colorless amorphous precipitate formed. The reaction mixture was then warmed to room temperature, the precipitate filtered, the ether distilled through a column, and the residue fractionated. After a careful distillation, in addition to the excess of PBr_3, there was isolated a 9.5 g fraction with b.p. 70° at 4 mm and d_{20}^{20} 2.6357.

5.995 mg, 3.825 mg substance: 1.212 mg, 0.775 mg CO_2; 0.775 mg, 0.411 mg H_2O. 14.4 mg, 17.97 mg substance: 7.362 ml, 9.386 ml 0.02 N $AgNO_3$. 0.2838 g, 0.2880 g substance: 20.72 ml, 19.02 ml 0.1 N $AgNO_3$. 0.1894 g, 0.1810 g substance: 0.2363 g, 0.1987 g molybdate. Found %: C 5.51, 5.52; H 1.14, 1.20; Total Br 83.20, 83.47; hydrolyzable Br 58.34, 58.91; P 9.20, 10.95; $BrCH_2PBr_2$. Calculated %: C 4.22; H 0.70; total Br 84.40; hydrolyzable Br 56.25; P 10.85.

Bromomethyldibromophosphine was obtained in a 50% yield based on the diazomethane. When the ratio PBr_3: CH_2N_2 = 2:1 and PBr_3: CH_2N_2 = 1:1, the amount of the precipitate increased sharply and the yield of the $BrCH_2PBr_2$ dropped until, in the latter case, it was only 15-20%. The residue was readily hydrolyzed in the air with the formation of bromine; it was soluble in water and in alcohols, and insoluble in benzene, carbon tetrachloride, and chloroform. It decomposed on recrystallization. The substance was an organophosphorus compound.

15. Oxidation of bromoethyldibromophosphine with nitrogen dioxide. The acid bromide of bromomethylphosphinic acid, $BrCH_2POBr_2$. 4.9 g of dry NO_2 was passed, over a period of 25 min at 5-10°, into a solution of 17 g of $BrCH_2POBr_2$ in 50 ml of dry CCl_4. At the start of the passage of the gas, a precipitate formed which dissolved at the end of the reaction, whereupon the temperature of the reaction mixture began to rise. After standing for a half hour at room temperature, the nitrogen dioxide and the solvent were removed in vacuum and the residue fractionated. Weight of the product – 10.8 g; it distilled at 118-120° at 7 mm or 112-113° at 2 mm. It was a solid substance, m.p. 38°, which readily supercooled. The constants of the supercooled substance were: d_{20}^{20} 2.7030, n_D^{20} 1.5120. Yield – 60% of the theoretical based on the phosphine.

0.2972 g, 0.2075 g substance: 19.91 ml. 13.85 ml 0.1 N. $AgNO_3$. 0.6510 g substance; 16 g benzene; Δt 0.6650. Found %: hydrolyzable Br 53.53, 53.34; M 315.0. $BrCH_2POBr_2$. Calculated %: hydrolyzable Br 53.15; M 300.5. Bromomethyldibromophosphine reacted energetically with metallic mercury to form a compound which could not be vacuum distilled.

16. Diethyl ester of bromomethylphosphinic acid – $BrCH_2PO(OC_2H_5)_2$. A mixture consisting of 20 ml of ether and 3.4 g ofabsolute alcohol was added, dropwise in the cold (ice and salt), to 10.8 g of the acid bromide, $BrCH_2POBr_2$, in 40 ml of dry ether followed by a solution of 10.3 g of diethylaniline in 50 ml of ether; the reaction mixture was allowed to stand over night at room temperature.

The precipitate of diethylaniline hydrobromide was filtered and carefully washed with ether. After distillation of the ether from the filtrate, the residue was fractionated. The diethyl ester of bromomethylphosphinic acid, b.p. 99° at 1 mm, was obtained in a yield of 50% based on the weight of the acid bromide.

d_{20}^{20} 1.4474; n_D^{20} 1.4585.

0.1620 g substance: 1.36 ml 0.1 N. $AgNO_3$. 0.433 mg, 0.391 mg substance; 21.99 ml 20.00 ml 0.1 N. $Na_2S_2O_3$. Found %: Br 33.62; OC_2H_5 37.79, 38.15. $BrCH_2PO(OC_2H_5)_2$. Calculated %: Br 34.59; OC_2H_5 38.93.

17. Bromomethylphosphinic acid – $BrCH_2PO(OH)_2$. 2g of $BrCH_2POBr_2$ was hydrolyzed by means of 3 ml of water. The excess water was removed in a vacuum desiccator over P_2O_5. The acid was very hygroscopic, and it was very difficult to identify it; for this reason, it was transformed into the aniline salt by addition of an excess of aniline to a solution of the acid in benzene. Upon recrystallization of the salt from alcohol containing 1% aniline, thin needles, m.p. 187° (with decomp.) were obtained. The yield was theoretical.

4.403 mg, 4.495 mg substance: 0.2087 ml, 0.1960 ml N_2 (32°, 747 mm). 0.0809 g substance: 5.90 ml 0.1 N KOH (phenolphthalein).

Found %: N 5.19, 4.90; equiv. 137. $BrCH_2PO(OH)_2 \cdot C_6H_5NH_2$. Calculated %: N 5.22; equiv. 134.

18. Reaction of diazomethane and diazoethane with phosphorus oxychloride. An ether solution of 13-14 g of dry diazomethane* in 400 ml of ether was added stepwise to 120 g of $POCl_3$ diluted with 50 ml of ether at -25 to -30° in the presence of dry copper sulfate (at first 1 g was added, and then 0.5 g was added twice during the course of the experiment. After the formation of the nitrogen stopped, the reaction mixture was allowed to come to room temperature, the ether was distilled through the column, and the residues from three such experiments were combined and distilled. After removal of the $POCl_3$ and a careful distillation of the residues, 6 g of a fraction, b.p. 59.5° at 12 mm, was obtained.

Found %: C 8.78, 8.73; H 2.24, 2.54; total Cl 46.88, 46.85; hydrolyzable Cl 46.89, 46.87; P 22.19, 22.28; M 146.1. CH_3OPOCl_2. Calculated %: C 8.05; H 2.02; Total Cl 47.65; hydrolyzable Cl 47.65; P 20.81; M 149.

Therefore, the product was the methyl ester of dichlorophosphoric acid. Literature constants: b.p. 62-64° at 14 mm [8].

The ethyl ester of dichlorophosphoric acid (2.5 g), b.p. 163-165°, was obtained in an analogous manner from $POCl_3$ (15.5 g) and diazoethane (8.5 g).

Found %: Total Cl 43.89; Hydrolyzable Cl 43.03; M 159. $C_2H_5OPOCl_2$. Calculated %: Total Cl 43.55; Hydrolyzable Cl 43.55; M 163. Thesubstance – the ethyl ester of dichlorophosphoric acid – was described in the literature [8]: b.p. 167° (with decomp.).

* The diazomethane was dried initially in the usual manner at a temperature of -70° over solid KOH and then over sodium ribbon.

19. Reaction between diazomethane and PCl_5. Trichloromethyl phosphine oxide $(ClCH_2)_3PO$. A solution of 6 g of diazomethane in 200 ml of ether dried in the usual manner over KOH with cooling, was added, dropwise with mechanical stirring, at -40°, to a mixture of 10 g of PCl_5 and 40 ml of dry ether. At end of the formation of the nitrogen, the cooling was removed and the solution was left overnight. The ether solution was poured from the precipitate, which was then extracted with ether (2 times with 50 ml). After the removal of the ether, 6-7 g of needlelike crystals separated, which after recrystallization from gasoline, melted at 100.5°. The product did not contain any chlorine that could be hydrolyzed under ordinary conditions.

Found %: C 18.43, 19.00; H 3.25, 3.43; Cl 54.24; P 15.21, 15.59; M 188. $(ClCH_2)_3PO$. Calculated %: C 18.41; H 3.07; Cl 54.53; P 15.87; M 195.5.

Reported (as the semihydrate) by Hoffmann: m.p. 88-89° [6].

20. Reaction of diazoethane with PCl_5. A dry solution of 14-15g of diazoethane (5 moles) in 400 ml of ether, dried over KOH and then over sodium ribbon, was added (efficient mechanical stirring) at -40 to -50° to 10 g (1 mole) of finely ground PCl_5 in 50 ml of absolute ether. The last portions of the diazoethane decolorized slowly. The solution, containing unreacted diazoethane, was allowed to stand over night at room temperature. All of the PCl_5 dissolved. After distillation of the ether, 10 g of a viscous, cloudy liquid, difficultly soluble in water, containing hydrolyzable chlorine, was obtained. The vacuum distillation (5 mm) of the substance was accompanied by noticeable decomposition, and a homogeneous product could not be isolated. A liquid, b.p. 55-115° at 5 mm, 4.5 g was collected together and hydrolyzed with 5 ml of hot water (very little dissolved in cold water). After 2-3 days, the oily layer was extracted. The water layer was then extracted with ether, the ether extract dried with sodium sulfate, and the ether distilled. The residual oil crystallized on standing in the desiccator. The thin needles were pressed on a plate and recrystallized from a mixture of benzene and gasoline, m.p. 107°. 1.5 g was obtained; it was moderately soluble in water and very soluble in alcohol.

4.614 mg substance: 4.278 mg CO_2; 2.075 mg H_2O. 11.700 mg substance: 6.058 ml 0.02 N $AgNO_3$. Found %: C 25.28; H 5.03; Cl 36.72. $(CH_3CHCl)_2PO(OH)$. Calculated %: C 25.13; H 4.18; Cl 37.17.

The silver salt of di α-chloroethyl-phosphinic acid was water soluble.

21. Aniline salt of di(α-chloroethyl)phosphinic acid. 3 ml of aniline was added to a solution of 2 g of $(CH_3CHCl)_2PO(OH)$ in 50 ml of benzene. The salt precipitated in the form of needles, which decomposed on melting at 160°. The yield was quantitative.

2.815 g substance: 0.1430 ml N_2 (28°, 738 mm). Found %: Cl 5.48.

$(CH_3CHCl)_2PO(OH) \cdot C_6H_5NH_2$. Calculated %: N 4.93.

SUMMARY

1. It was shown that the diazo method for the synthesis of organo-elemental compounds could be successfully extended to the preparation of organophosphorus compounds.

2. Phosphorus trichloride and phosphorus tribromide, when reacted with diazomethane, diazoethane, and diazobutane, formed the corresponding primary α-halodialkylphosphorus compounds, whose properties and derivatives are reported.

3. Phosphorus pentachloride with diazomethane and diazoethane formed the corresponding secondary and tertiary α-halodialkyl phosphorus derivatives. Phosphorus oxychloride and bromide did not form any compounds containing a C-P bond under analogous conditions.

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TRANSFORMATION OF CYCLOPENTENE BY THE ACTION OF ALUMINUM CHLORIDE

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On studying the action of aluminum chloride on cyclohexene, it was found that the reaction proceeded mainly in the direction of the formation of hydropolymers. A small amount of cyclohexene resisted the dehydrogenation and, as a result, tetracyclohexylbenzene [1] was formed. When the investigation of the polymerization of cyclopentene in the presence of aluminum chloride was started, the formation of hydro-and dehydropolymers was also expected; but apparently, when aluminum chloride reacted with cyclopentene, more complex reactions occurred and did not lead to the formation of polymers.

The polymerization of cyclopentene was conducted at 50° with 20% of the catalyst. When the reaction products were distilled, a series of fractions were obtained, corresponding, in molecular weight, to dimers, trimers, and tetramers, but different in their constants, from polycyclopentyls and polycyclopentylcyclopentene, which had been previously obtained synthetically and were reported in the literature [2-7].

The fraction, b.p. 185-186° at 748 mm, corresponding in molecular weight to the dimer, was a colorless liquid with an odor resembling that of the terpenes. In spite of its high boiling point this substance was very volatile. Its constants were very close to the constants of spirocyclodecane (Tables 1 and 2).

Heptabromospirocyclodecane, b.p. 252.5-253.5°, was prepared by the action of bromine on the above spirocyclodecane. No depression was obtained in a mixed melting point determination with heptabromospirocyclodecane prepared from synthetic spirocyclodecane.

Spirocyclodecane, has, up to now, been prepared synthetically. Zelinsky and Shuikin [7], synthesized it from 1,1'-di-hydroxydicyclopentene; Marvel and Brooks [8] by the cyclization of penta-1,4-dienylcyclopentane followed by hydrogenation. Several spirans have been obtained by means of aluminum chloride but all of these were formed by the isomerization of alicyclic olefins containing substituted arylalkyls in the molecule. The ring was obtained by the fusion of the aromatic ring to the alicyclic olefin at the double bond.

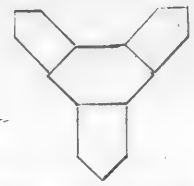
TABLE 1

Name	Formula	Melting point	n_D^{20}	d_4^{20}	Iodine number
Spirocyclodecane	$C_{10}H_{18}$	185-186° 748 mm	1.4740	0.8827	2.87
Tricyclopentane	$C_{15}H_{24}$	127-129 4.5 mm	1.5085	0.9606	2.63
Tetracyclopentane	$C_{20}H_{32}$	198-200 4.5 mm	1.5295	1.0028	3.5
Hexacyclopentene	$C_{30}H_{48}$		—	—	36.2

Thus, the possibility of forming spirocyclodecane by the polymerization of cyclopentene in the presence of aluminum chloride was shown in this investigation. It is believed that a dimer is formed during the polymerization, one ring of which, under the isomerizing action of aluminum chloride, is transformed into a six-membered ring at the carbon atom of the other five-membered ring. Since it is energetically impossible to transform a five membered ring into a four-membered one [9] in this case, a system of a five-membered and six-membered ring with one common carbon atom is formed—spirocyclodecane.

The fraction, b.p. 127-129° at 4.5 mm, according to its molecular weight, was tricyclopentane with an iodine number of 2.63 (Table 1). This substance can practically be considered saturated because, with one

double bond, it would have had an iodine number of 124.5. The elementary analysis corresponded to the formula $C_{15}H_{24}$. The following structure is considered to be probable for this compound:



The fraction with b.p. 198-200° at 4.5 mm and iodine number 3.5, was the tetramer, according to its molecular weight. A formula $C_{20}H_{32}$ was calculated from the elementary analysis, whereas, the formula $C_{20}H_{34}$ corresponds to the saturated tetramer. The iodine number was insignificant. Apparently, as in the case of the trimer, the lack of two hydrogens was not due to the presence of a double bond (theoretical iodine number 83.4), but was a result of the fusion of rings to form a new ring.

TABLE 2

Reference	Boiling point	n_D^{20}	d_4^{20}	MR_D	
				Calculated	Found
[7]	185-186°	1.4748	0.8877	43.98	43.74
[8]	184-186.5	1.4744	0.8805	43.98	44.14
Our results	185-186	1.4740	0.8827	43.98	43.98

The fraction, b.p. 190-220° at 3 mm was a very dense oil with a very abrupt temperature-viscosity curve. Viscosity index: −55. This fraction was not studied in detail.

After distillation of the polymerization products there always remained in the flask a large amount of a glasslike solid residue, which, by means of recrystallization from isopropyl alcohol, gave a finely crystalline substance, m.p. 71-72° and an iodine number 36.2 (Margosches). Further investigation showed that it was the hexamer of cylcopentene, $C_{30}H_{48}$, containing one double bond.

EXPERIMENTAL

Cyclopentene was obtained by the dehydration of cyclopentyl alcohol with orthophosphoric acid at 240°. It had a b.p. of 44°, d_4^{20} 0.7715; n_D^{20} 1.4231.

The apparatus for the polymerization was equipped with a mercury sealed stirrer and an efficient coil condenser connected to a trap immersed into a dish of solid carbonate. The polymerization of cyclopentene was effected at 50° for 30 hours with 20% $AlCl_3$. In spite of the rapid formation of the complex of cyclopentene and aluminum chloride, the rate of polymerization was very slow. and it was necessary to conduct the process at room temperature for 2 days, for 3 hours at 35°, and for 27 hours at 50°. At the end of the polymerization, the upper layer was separated from the solid (complex) lower layer. After washing and drying, the upper layer was fractionated at ordinary pressure and in vacuum. A solid residue, the main portion of the products, remained in the flask.

6 experiments on the polymerization of cyclopentene were conducted. In all cases, the yield of the fraction boiling up to 200° did not exceed 5%; 50% of the product was distributed amont fractions boiling from 80 - 235° at 5 mm. The residue, amounting to 45%, was a solid product.

For example: 74 g of cyclopentene and 14.8 g of $AlCl_3$ were heated for 30 hours at 50°. 50 g of an upper layer was obtained, which on distillation, gave the following fractions: at 748 mm 182-193° −2.6 g; at 5 mm 80-195° −13.4 g, 195-235° −12.2 g (oil), 235-260° −10.2 g (solid), and residue −11.6 g.

All of the polymerization products had low iodine numbers which in several cases were equal to zero. The smallest values were found for the lower fractions. The higher boiling fractions had higher iodine values.

After many refractionations, the following fractions were obtained and studied: b.p. 185-187° at 743.7 mm; b.p. 125-129° at 4 mm; b.p. 197-209° at 5 mm; b.p. 190-220° at 3 mm; and a solid residue.

Spirocyclodecane. After a careful distillation of the fraction, a product, b.p. 185-187° at 743.7 mm, was isolated. It was very volatile and had a characteristic odor resembling that of the terpenes.

d_4^{20} 0.8906; n_D^{20} 1.4756. MR_D 43.71; calculated 43.98; iodine number 18.22.

The product b.p. 185-187°, was treated with one volume of sulfuric acid (density = 1.84) for 30 minutes to remove unsaturated impurities. A substance with the following constants was obtained from the acid-treated product:

B.p. 185-186° at 748 mm; d_4^{20} 0.8827; n_D^{20} 1.4740. MR_D 43.98; calculated 43.98; iodine number 2.87.

2.727 mg substance: 8.665 mg CO_2; 3.192 mg H_2O. 2.617 mg substance; 8.320 mg CO_2; 3.130 mg H_2O. 0.1658 g substance; 19.85 g benzene: Δt 0.315°. 0.2617 g substance; 19.85 g benzene: Δt 0.514°. Found %: C 86.71, 86.76; H 13.10, 13.38; M 135.8, 136.3. $C_{10}H_{18}$. Calculated %: C 86.87; H 13.3; M 138.14.

This hydrocarbon was spirocyclodecane according to these constants.

The spirocyclodecane was brominated (according to Gustavson). The bromide, after recrystallization from benzene, was obtained in the form of soft needles, m.p. 252.5-253.5°.

0.0365 g substance: 0.0696 g AgBr (Carius); 0.0562 g substance: 0.1064 g AgBr. Found %: Br 81.14, 80.57. $C_{10}H_{11}Br_7$. Calculated %: Br 81.02.

A smooth analysis was obtained only with small samples. When the size of the sample was increased, the tubes usually exploded. The spirocyclodecane heptabromide was identical with the synthetic spirocyclopentyl heptabromide prepared by N.V. Elagena at Moscow State University. The synthetic spirocyclodecane (cyclopentenspirocyclohexane) had an m.p. of 250°. The mixed melting point with spirocyclodecane heptabromide obtained from the polymerization of cyclopentene did not give any depression.

Tricyclopentane. A narrow boiling fraction, b.p. 125-129° at 4.5 mm, was isolated from the fraction with b.p. 80-195° at 5 mm by means of a large number of redistillations: d_4^{20} 0.9622; n_D^{20} 1.5098; ... iodine number 13.84.

The product was treated three times with one volume of sulfuric acid (d = 1.84) to remove the unsaturated compounds. Each of the sulfonations lasted 30 minutes. After neutralizing and drying, the product was distilled and a fraction, b.p. 127-129° at 4.5 mm, was isolated from it. It had the following constants:

d_4^{20} 0.9606; n_D^{20} 1.5085. MR_D 63.41; calculated 62.67.

3.015 mg substance: 9.715 mg CO_2; 3.258 mg H_2O. 2.572 mg substance: 8.300 mg CO_2; 2.730 mg H_2O. 0.1492 g substance; 20.45 g benzene: Δt 0.185°. 0.2488 g substance; 20.45 g benzene: Δt 0.308°, Found %: C 87.93, 88.07; H 12.09, 11.88; M 201.9, 202.2. $C_{15}H_{24}$. Calculated %: C 88.15; H 11.85; M 204.19.

Tetracyclopentane. $C_{20}H_{32}$. The fraction with b.p. 197-202° at 5 mm, was treated 5 times with one volume of sulfuric acid (d = 1.84) to remove the unsaturated compound impurities. The iodine number decreased from 7.14 to 3.5.

The purified product had the b.p. 198-200° at 4.5 mm and the following constants:

d_4^{20} 1.0028; n_D^{20} 1.5295. MR_D 83.76; calculated 83.56.

2.530 g substance: 8.170 mg CO_2; 2.710 mg H_2O. 2.520 mg substance: 8.135 mg CO_2; 2.712 mg H_2O. 0.2350 g substance; 21.26 g benzene: Δt 0.212°. 0.3764 g substance; 21.26 g benzene: Δt 0.340°. Found %: C 88.12, 88.10; H 11.98, 12.04; M 267.0, 266.6. $C_{20}H_{32}$. Calculated %: C 88.15; H 11.85; M 272.26.

The fraction with b.p. 190-220° at 3.5 mm was an oil which had the following constants:

d_4^{20} 1.0038; n_D^{20} 1.5322; iodine number 9.24; M 291.8.

2.688 mg substance: 8.675 mg CO_2; 2.900 mg H_2O. 2.853 mg substance: 9.200 mg CO_2; 3.075 mg H_2O. Found %: C 88.07, 88.00; H 12.07, 12.06.

Viscosity at 50° – 80.49 cst., at 100° – 9.01 cst. (E_{50} 10.6; E_{100} 1.75). Viscosity index – 55. Freezing point -3°.

Hexacyclopentene. A finely crystalline substance, m.p. 71-72°, and iodine number (Margosches) 36.2, was obtained after the recrystallization of the solid residue from isopropyl alcohol. The theoretical iodine number for $C_{30}H_{48}$ is 62.20. The decrease in the iodine number, apparently, was due to the instability of the iodide of hexacyclopentane.

2.610 mg substance: 8.425 mg CO_2; 2.770 mg H_2O. 2.471 mg substance: 7.974 mg CO_2; 2.618 mg H_2O. 0.0919 g substance; 19.23 g benzene: Δt 0.060°. 0.0818 g substance; 24.60 g benzene: Δt 0.048°. Found %: C 88.09, 88.07; H 11.88, 11.86; M 407.8, 398.1. $C_{30}H_{48}$. Calculated %: C 88.15; H 11.85; M 408.38.

Therefore, this product is a hexacyclopentene containing one double bond.

SUMMARY

A complex mixture of hydrocarbons results from the reaction of cyclopentene with aluminum chloride, from

which spirocyclodecane, tricyclopentane, tetracyclopentane, and hexacyclopentene was isolated.

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PREPARATION OF DIMETHYL PYROCARBONATE

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The literature reports the synthesis of four examples of esters of the hypothetical pyrocarbonic acid; diethyl pyrocarbonate, di-n-propyl pyrocarbonate [1], di-n-butyl pyrocarbonate [2], and methyl ethyl pyrocarbonate [3]. The attempts of Boehm and Mehta to prepare dimethyl pyrocarbonate by their method failed. The negative results of the experiments were explained by these authors as being due to the thermal instability of dimethyl pyrocarbonate, which, during the isolation of the crude product by vacuum distillation, completely decomposed into carbon dioxide and dimethyl carbonate.

The method of Boehm and Mehta was followed closely in the experiment conducted to verify this conclusion, the only difference being that the vacuum distillation of the crude product was replaced by one at ordinary pressure, because the decomposition products of dimethyl pyrocarbonate could more easily and accurately be determined in this fashion. The formation of carbon dioxide and dimethyl carbonate occurred only in insignificant amounts. The main fraction obtained was methyl alcohol. Apparently, dimethyl pyrocarbonate was present in the crude reaction product. It must be pointed out that the method of Boehm and Mehta is based on the reaction of chlorocarbonic esters with emetine in chloroform, and the saponification of the carboalkoxy derivatives of emetine with aqueous potassium hydroxide. Under their conditions, the formation of methyl alcohol is possible, either by the saponification of the carbomethoxy derivative of emetine at the ester linkage, or by the saponification of the initially formed dimethyl pyrocarbonate. In any case, it is clear that the reason for the negative results in the synthesis of dimethyl pyrocarbonate by this method, was the presence of a strong hydrolyzing agent in the reaction medium. Dimethyl pyrocarbonate must be more susceptible to hydrolysis than diethyl pyrocarbonate, since the latter is obtained in good yield by the method of Boehm and Mehta.

A new method for the preparation of pyrocarbonic esters was suggested by the authors [3], which was based on the reaction of the alkali salts of alkyl carbonic acid with chlorocarbonic esters. It excluded the presence of hydrolyzing factors in the reaction medium. It was shown that the considerable increase in yield of diethyl pyrocarbonate by this synthesis over that of Boehm and Mehta, was due to this fact. Experiments conducted to develop this method led to fully satisfactory yields of up to 64% of the theoretical.

Dimethyl carbonate was a colorless, readily volatile oil, with a pleasant, slightly sharp odor, insoluble in water, but readily soluble in ether, alcohol and benzene. In contrast to all of the pyrocarbonates prepared up to now, dimethyl pyrocarbonate crystallized readily on cooling.

The structure of dimethyl pyrocarbonate is established by its formation from the reaction between alkali salts of methyl carbonic acid and methyl chlorocarbonate (Equation 1), by its decarboxylation on pyrolysis (Equation 2), and by its reaction with ammonia and aniline to form the corresponding urethane and phenyl urethane (Equations 3 and 4).

$$CH_3O{-}CO{-}ONa + Cl{-}CO{-}OCH_3 \longrightarrow CH_3O{-}CO{-}O{-}CO{-}OCH_3 + NaCl \quad (1)$$

$$CH_3O{-}CO{-}O{-}CO{-}OCH_3 \xrightarrow{123\text{-}149^\circ} CH_3O{-}CO{-}OCH_3 + CO_2, \quad (2)$$

$$CH_3O{-}CO{-}O{-}CO{-}OCH_3 + NH_3 \longrightarrow CH_3O{-}CO{-}NH_2 + CH_3OH + CO_2 \quad (3)$$

$$CH_3O{-}CO{-}O{-}CO{-}OCH_3 + C_6H_5NH_2 \longrightarrow CH_3O{-}CO{-}NHC_6H_5 + CH_3OH + CO_2 \quad (4)$$

A comparative study of the hydrolysis of dimethyl and diethyl pyrocarbonate showed that dimethyl pyrocarbonate hydrolyzed much more rapidly than diethyl pyrocarbonate.

The following equations are proposed on the basis of the study of hydrolysis in water and aqueous alkali:

$$RO{-}CO{-}O{-}CO{-}OR + HOH \longrightarrow 2ROH + 2CO_2,$$

$$RO{-}CO{-}O{-}CO{-}OR + 4KOH \longrightarrow 2ROH + 2H_2CO_3 + H_2O.$$

Dimethyl pyrocarbonate is less stable thermally than diethyl pyrocarbonate.

EXPERIMENTAL

1. Synthesis of dimethyl pyrocarbonate by the method of Boehm and Mehta. The methyl chlorocarbonate necessary for the synthesis was prepared by the method of Dumas [4]. The boiling point of the ester (71-72°) corresponded to the literature value. A solution of 1 g of emetine hydrochloride (pharmacopoeia preparation) in 30 ml of chloroform and 4.7 g of methyl chlorocarbonate were mixed in a separatory funnel. 27 ml of a 10% aqueous potassium hydroxide was added, with good shaking and water cooling, in three 9-ml portions, to this mixture. After addition of all the alkali, the reaction mixture was slightly alkaline. The chloroform layer was separated and the chloroform distilled on the water bath; the residue, after removal of the chloroform, was processed with ether; a yellow precipitate formed and was filtered off; the filtrate was treated with dilute hydrochloric acid. The ether layer was then separated and dried over fused sodium sulfate for several hours; the ether was distilled and the residue fractionated in vacuum. 2 - 3 drops of a liquid distilled at 55° and 8 mm.

In other experiments, the residue obtained after the distillation of the ether was fractionated at ordinary pressure. A large portion of the liquid distilled at 60-68° (methyl alcohol) and an almost insignificant amount — several drops in all — at 90-91° (dimethyl carbonate); during the distillation there was a constant evolution of a small amount of carbon dioxide.

2. Synthesis of dimethyl pyrocarbonate from methyl chlorocarbonate and sodium methylcarbonate. Methyl chlorocarbonate was prepared in the same way as in the previous case. Sodium methyl carbonate was prepared by passing dry carbon dioxide into a solution of sodium methylate in methyl alcohol. The purity of the salt was shown by its analysis for sodium content: found 23.42% sodium; calculated 23.37%. A mixture of 9.8 g of sodium methylcarbonate and 37 g of methyl chlorocarbonate was placed into a 100-120 ml tall beaker, equipped with a reflux condenser with a calcium chloride tube and a mercury-sealed, mechanical stirrer. The reaction mixture was then filtered through a Buchner funnel and the residue washed with a small amount of dry ether. After removal of the ether, the filtrate was fractionated in vacuum. The excess chlorocarbonic ester distilled at 25-30° at 110 mm; the residue distilled completely at 45-46° and 5 mm. Yield 8.5 g or 63.43% of the theoretical. When it was cooled with ice water and shaken, the ester rapidly crystallized in the form of colorless prisms.

Freezing point 15.2°; d_4^{20} 1.2585; n_D^{20} 1.3950.

0.2108 g substance: 0.2768 g CO_2; 0.0836 g H_2O. Found %: C 35.81; H 4.44. $C_4H_6O_5$. Calculated %: C 35.84; H 4.51.

3. Pyrolysis of dimethyl pyrocarbonate. The pyrolysis was effected in a 4-5 ml flask with a ground-in, well-fitted, reflux condenser, the top of which was connected to a potassium hydroxide apparatus. The neck of the flask was closed with a two-hole stopper. Through one of the holes a thermometer was fitted with its bulb almost touching the bottom of the flask, and in the other hole, a glass tube with a valve for the passage of air. 3.70 g of dimethyl pyrocarbonate was weighed into the flask. After passing dry, carbon dioxide-free air through the apparatus for 15 minutes, it was connected to the potassium hydroxide apparatus containing 50% potassium hydroxide. The flask was heated on a glycerin bath. Bubbles of gas started forming in perceptible amounts, and rapidly increased, at 123°. The temperature of the liquid in the flask gradually rose to 149° and then began to drop; at 95°, the evolution of the CO_2 ceased. 1.20 g of carbon dioxide was collected; calculated from the equation of the pyrolysis: 1.21 g; the residue in the flask weighed 2.41 g; the calculated weight of the dimethyl carbonate from the pyrolysis equation was 2.48 g.

The residual liquid in the flask distilled completely at 90-91°, which corresponded to the boiling point reported in the literature for dimethyl carbonate [5].

Found %: C 39.89; H 6.80. $C_3H_6O_3$. Calculated %: C 40.00; H 6.71.

4. Pyrolysis of diethyl pyrocarbonate. The pyrolysis of diethyl pyrocarbonate was effected in the same apparatus and under the same conditions as the pyrolysis of dimethyl pyrocarbonate. The formation of the gas bubbles was perceptible at 155°; the temperature of the liquid gradually rose to 175° and then began to fall; at 130°, the evolution of carbon dioxide ceased.

Sample of diethyl pyrocarbonate - 4.75 g; collected CO_2 - 1.24 g; calculated from the pyrolysis equation 1.29 g. The residue in the flask weighed 3.40 g; calculated amount of diethyl carbonate from the pyrolysis equation 3.46 g. The residue in the flask distilled completely at 125-126°, which corresponded to the distillation temperature of diethyl carbonate.

5. Urethane (methyl ester of carbamic acid). A saturated solution of ammonia in ethyl alcohol was added to 1 g of dimethyl pyrocarbonate. The reaction started and continued rapidly. The mixture heated up and carbon dioxide was given off. The ammonia was added until the evolution of the carbon dioxide ceased. After evaporation of the alcohol, colorless crystals remained, which were dried in a desiccator over calcium chloride. M.p. 52-53°; according to Gattermann [7], 52°; according to Schmidt [8], 54.2°.

Found %: N 18.35. $C_3H_5O_2N$. Calculated %: N 18.65.

The reaction proceeded much more violently with gaseous ammonia.

6. Phenyl urethane (methyl ester of phenyl carbamic acid). 1 g of dimethyl pyrocarbonate was added, dropwise, to 0.7 g of freshly distilled aniline. The reaction started and proceeded rapidly, with the mixture heating up and the evolution of carbon dioxide. After cooling, the mixture crystallized completely, either when it was shaken, or when it was seeded with a crystal of phenyl urethane. The yield was quantitative. On recrystallization from hot water, the phenyl urethane was obtained in the form of scaly crystals, m.p. 47°, which agreed fully with the literature [9].

7. Hydrolysis of dimethyl pyrocarbonate and diethyl pyrocarbonate. The apparatus used for the hydrolysis consisted of a beaker [a] 50-75 ml in volume, fitted with a mercury-sealed, mechanical stirrer and two connected burets fitted to the beaker by means of glass tubes. A saturated solution of sodium chloride, which was equal to one-half the total volume of the burets (with a small excess), was placed into the burets. One of the burets (b), fitted with a three-way stopcock, was used to collect the carbon dioxide generated during the hydrolysis, the other (c) was always left open to the atmosphere in order to level the liquid in the first buret to zero and to keep the pressure inside the apparatus equal to that of the atmosphere. The experiments were performed at room temperature (15°). In order to exclude the influence of the variation in temperature, the beaker was placed in a constant temperature water bath.

a) 10 ml of distilled water was placed in the beaker and initially saturated with carbon dioxide for 10 minutes. The liquid level in the first buret was brought to zero and the corresponding opening in the three way stopcock placed at "closed" position. The stirrer was allowed to run (100-120 r.p.m.). After the excess carbon dioxide stopped separating, the stirrer was stopped and 0.0618 g of dimethyl pyrocarbonate was introduced through the side tube with a special pipet. The side arm was plugged with a plastic stopper, the liquid in the first buret was again leveled to zero, and the stirrer allowed to run at the previous rate. The formation of carbon dioxide stopped after 90 minutes. A total of 20.3 ml (reduced to normal conditions) of gas was collected; calculated from the hydrolysis equation 20.6 ml.

Hydrolysis of dimethyl and diethyl pyrocarbonate

Time from beginning of expt. (minutes)	Formation of carbon dioxide on hydrolysis			
	Dimethyl pyrocarbonate		Diethyl pyrocarbonate	
	in ml	In % of the quantity calculated from the hydrolysis equation	in ml	In % of the quantity calculated from the hydrolysis equation
15	8.1	41.26	4.3	26.88
30	13.7	66.51	6.5	40.63
60	17.7	85.92	10.0	62.50
90	20.3	98.54	12.4	77.50
120	–	–	14.4	90.00
150	–	–	15.9	99.37

b) 0.0580 g of diethyl pyrocarbonate was hydrolyzed under approximately analogous conditions. The formation of the carbon dioxide ceased after 150 minutes. A total of 15.9 ml (reduced to normal conditions) of gas was collected; calculated from the hydrolysis equation – 16 ml.

The data on the dynamics of the formation of carbon dioxide are listed in the Table.

8. Hydrolysis of dimethyl pyrocarbonate and diethyl pyrocarbonate with aqueous potassium hydroxide. The aqueous solution of potassium hydroxide was 0.3685 N; 1 ml corresponded to 0.01294 g of dimethyl pyrocarbonate or 0.01493 g of diethyl pyrocarbonate.

a) 50 ml of potassium hydroxide solution was added rapidly to 0.2320 g of dimethyl pyrocarbonate with good stirring; the ester dissolved within the first minute. 10 ml of the solution was removed and rapidly titrated with hydrochloric acid.

The titration was effected according to Warder [10]. 18.5 ml of potassium hydroxide, corresponding to 0.2287 g of dimethyl pyrocarbonate, was consumed during the saponification. The ester hydrolyzed to an extent of 93.4%.

b) A 0.3983 g sample of diethyl pyrocarbonate was saponified with the alkali under the same conditions as the dimethyl pyrocarbonate. 26 ml of potassium hydroxide, corresponding to 0.3882 g of diethyl pyrocarbonate, was consumed during the saponification of the ester. Diethyl pyrocarbonate hydrolyzed to an extent of 98.8%.

SUMMARY

1. A method is given for the preparation of dimethyl pyrocarbonate, which is not reported in the literature.

2. The comparative characterization of dimethyl- and diethyl- pyrocarbonate, on the basis of thermal and hydrolysis stability, is given.

3. A new method for the preparation of urethane and N-substituted urethanes is given.

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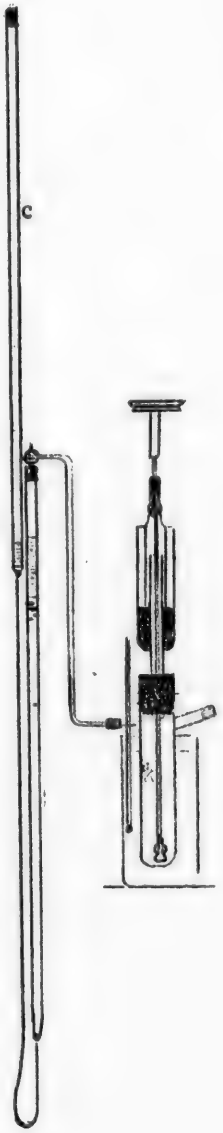
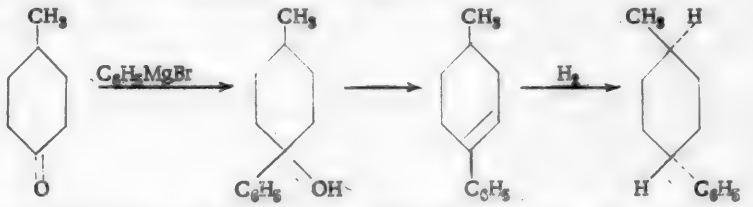


CYCLIZATION OF AROMATIC COMPOUNDS

V. SYNTHESIS OF 1-METHYL-4-PHENYLCYCLOHEXANE

N. G. Sidorova and A. D. Grebenyuk

There are many difficulties in the investigation of the condensation products of isomeric methylcyclohexanols and benzene because of the possibility of many isomeric and stereoisomeric forms, and the lack of study of this series of hydrocarbons. The synthesis of individual "model" hydrocarbons is of considerable importance for decreasing the difficulties in the investigation of structure and configuration of the condensation products. One of these hydrocarbons, -trans-1-methyl-4-phenylcyclchexane was synthesized in the following manner:



This method was generally used for the synthesis of substituted cyclohexyl hydrocarbons. A 1-methyl-4-phenylcyclohexane, of unknown configuration was synthesized in this manner [1]. The last part of this synthesis – the hydrogenation – was effected by these authors at 36° and 85 atm. of hydrogen over nickel on kieselguhr. It is believed that at such low temperature, the cis product was formed mainly, or almost exclusively.

When aromatic compounds or cycloalkenes are hydrogenated, the preference of one form over the other depends on the medium and the temperature. Skita [2], generalizing a large amount of experimental material on hydrogenation with platinum catalysts, proposed rules for the effect of the media on the configuration of the hydrogenation product; hydrogenation in acidic media preferably leads to the formation of the cis isomer and in basic or neutral media to the trans isomer. The preference of one form over the other also can depend on the temperature. For example, Zelinsky and Margolis [3], upon the hydrogenation of o- and p-acids over osmium catalysts at 50 - 70°, obtained cis-dimethylcyclohexanes and at 150° mixtures of stereoisomers with considerable amounts of the trans forms. The effect of the temperature on the direction of the hydrogenation with platinum on carbon can also be seen in the work of Kazansky, et al, on the synthesis and hydrogenative cleavage of cyclodi- and tri-substituted cyclopentenes. On the synthesis of 1,2-dimethyl and 1,2,3-trimethylcyclopentanes [4,5], by hydrogenation of the corresponding cyclo-olefins at 130-140°, a mixture of cis and trans isomers was obtained. On hydrogenation of each of the stereoisomeric 1,2,3-trimethylcyclopentenes with the same catalyst at 300-310°, along with hydrogenolysis, mutual steric rearrangements took place which favored the complete formation of the trans form [6]. The results of the hydrogenation with nickel will probably also depend on the temperature.

The hydrogenation of cyclic hydrocarbons with nickel at 180° usually leads completely to, or favors, the trans form [7]. For this reason, the above temperature was chosen for the hydrogenation of 4-methyl-1-phenylcyclohexene with Raney nickel. However, this high temperature is not completely convenient because, under these conditions, the aromatic ring also hydrogenates; for this reason, the hydrocarbons contained 1-methyl-4-cyclohexylcyclohexane as an impurity, as seen from the constants.

The synthesized hydrocarbon was characterized by the preparation of acetamino- and phenylamino derivatives, and by comparing them with the corresponding derivatives of the hydrocarbon obtained by the American chemists. The melting points of our derivatives of the hydrocarbon (see Table) were higher than the melting points of the corresponding derivatives of their hydrocarbon; indicating that the 1-methyl-4-phenylcyclohexane synthesized had the trans configuration.

Melting points of the derivatives of the stereoisomeric 1-methyl-4-phenylcyclohexanes.

Configuration	Acetoamino derivative	Phenylamino derivative
Cis isomer	142°	197°
Trans isomer	157 - 158	207 - 208°

However, the hydrocarbon probably was not the pure trans form because many recrystallizations of the derivatives were needed to obtain constant melting points.

EXPERIMENTAL

4-Methylcyclohexanol was obtained by the hydrogenation of p-cresol over Ni (Raney) at 180° and 120 atm. hydrogen pressure. B.p. 166-167° (720 mm). The subsequent steps in the synthesis differed somewhat in conditions and the yields from those reported in the literature [1].

4-Methylcyclohexanone. A solution of 40 g of sodium dichromate in 25 ml of H_2SO_4 and 90 ml of water was added, dropwise with stirring, to a solution of 45 g of 4-methylcyclohexanol heated to 40-50°. After the addition, the heating was continued for one hour at this temperature. The ketone was separated, washed with water, sodium carbonate solution, and again with water; and dried with $CaCl_2$ and distilled. The yield was 27.3 g (61.7% of theory). B.p. 169-169.5° (725 mm).

4-Methyl-1-phenylcyclohexanol. 26.6 g of 4-methylcyclohexanone was added dropwise over 3 hours to C_6H_5MgBr prepared from 48 g of phenyl bromide, 7.5 g of magnesium, and 120 ml of absolute ether; the mixture was then heated on the water bath for 2 hours. The decomposition was effected with dilute hydrochloric acid with ice cooling. The ether layer was separated, washed with water, dried with potassium carbonate, and after the removal of the ether, used directly for the next reaction without any further purification.

4-Methyl-1-phenylcyclohexene. The alcohol obtained in the above reaction was dehydrated by passing it over aluminum oxide deposited on pieces of unfused clay at 320-330° in 25-30 cm layers. The reaction product was dried over $CaCl_2$ and distilled. The yield of 4-methyl-1-phenylcyclohexene was 24.4 g (60 % of theory based on the ketone). B.p. 130-134° (15 mm).

Trans 1-methyl-1-phenylcyclohexane. 15 g of 4-methyl-1-phenyl-cyclohexane was dissolved in 10 ml of ethyl alcohol and mixed with 1.5 g of Ni (Raney) in an autoclave. The air in the autoclave was replaced with hydrogen and heating started. As soon as the temperature rose to 180°, 65 atm. of hydrogen was pumped in and the stirring started. The amount of hydrogen absorbed was somewhat greater than that theoretically calculated. After separation of the catalyst and removal of the alcohol, the product was distilled over metallic sodium.

B.p. 249-250° (727 mm); d_4^{20} 0.9277; n_D^{20} 1.5180; MR_D 56.88; calculated 56.43.

0.1196 g substance: 0.3912 g CO_2; 0.1120 g H_2O. Found %: C 89.22; H 10.40. $C_{13}H_{18}$. Calculated %: C 89.65; H 10.35.

According to the amount of hydrogen absorbed and the constants, it is seen that the hydrocarbon contained methylcyclohexylcyclohexane as an impurity.

For the characterization of trans 1-methyl-4-phenylcyclohexane, the entire product of the hydrogenation was nitrated, in the usual manner, without any initial separation, and the nitro compound was reduced with tin and hydrochloric acid. At the end of the reduction, the unreacted hydrocarbon and traces of the nitro compound were steam distilled. An excess of alkali was added to the residue, and the amine was steam distilled. The distillate was saturated with salt and the amine extracted with benzene. After drying with potassium hydroxide and removing the benzene, the amine was distilled. The yield of p-(4-methylcyclohexyl)aniline was 50.7% calculated on the hydrocarbon. B.p. 190-198° (at 38 mm).

Acetanilide – m.p. 157-158° (from dilute alcohol)

Benzanilide – m.p. 207-208° (from alcohol). 3.75 mg substance: 0.160 ml N_2 20.5°, (726 mm). Found %: N 4.74. $C_{20}H_{23}ON$. Calculated %: N 4.78.

SUMMARY

1. It was shown that the hydrogenation of 4-methyl-1-phenyl-cyclohexene at 180°, with Ni (Raney), favored the formation of the trans isomer of 1-methyl-4-phenylcyclohexane.

2. p-(Trans 4-methylcyclohexyl)acetanilide and benzanilide were prepared.

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ALLYLIC REARRANGEMENTS

XVII. REACTION BETWEEN ORGANO-MAGNESIUM COMPOUNDS AND ISOMERIC METHOXYCHLOROPENTENES

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In previous communications on the study of the reaction between organo-magnesium compounds and certain isomeric alkoxychloropentenes, it was shown that they proceed, to a great extent or fully, by the ionic mechanism. It was also shown that, varing with the nature of the radicals forming the organo-magnesium compounds and the isomeric alkoxycyclopentenes, mixtures of products are formed which differ considerably in their composition. For example, the reaction between phenyl magnesium bromide and the isomeric methoxychloropentenes leads to the formation of identical mixtures of isomeric methoxyphenylpentenes; whereas the reaction between phenyl magnesium bromide and the isomeric butoxychloropentenes gives only one product, 1-butoxy-5-phenylpent-3-ene, the primary chloride according to its structure.

The reaction of ethyl magnesium bromide and butyl magnesium with the isomeric ethoxychloropentenes and butoxychloropentenes leads to the formation of mixtures of two products, the corresponding 1-alkoxy-5-alkylpent-3-enes, derived from the primary form of the allyl halide, and the 1-alkoxy-6-β-alkoxyethyloct-3,7-dien, derived from the primary and secondary form of the allyl halide. The latter compounds are also formed by the direct action of metallic magnesium on the above isomeric alkoxychloropentenes; an abnormal bimolecular mechanism was proposed to explain their formation.

In the present study, the reaction between isomeric methoxychloropentenes, the most simple of the alkoxychloropentenes, and a series of organo-magnesium compounds was studied in order to obtain more detailed and more complete information on this theoretically interesting reaction, and to increase the amount of factual material. The organo-magnesium compounds used were benzyl magnesium chloride, ethyl magnesium bromide, and butyl magnesium bromide. Three products resulted from the action of benzyl magnesium chloride on 1-methoxy-5-chloropent-3-ene: 1-methoxy-3-benzylpent-4-ene, 1-methoxy-5-benzylpent-3-ene, and dibenzyl. The total yield of the isomeric methoxybenzylpentenes was 60.1%. 1-Methoxy-3-benzylpent-4-ene constituted 34.7% and 1-methoxy-5-benzylpent-3-ene 65.3% of the mixture. Similar results were obtained from the analogous reaction of benzyl magnesium with 1-methoxy-3-chloropent-4-ene. The total yield of the isomeric methoxybenzylpentenes was 51%; the mixture consisted of 35% of 1-methoxy-3-benzylpent-4-ene and 65% of 1-methoxy-5-benzylpent-3-ene. The formation of a considerable amount of dibenzyl occurred. The structure of these compounds was determined by oxidizing them with potassium permanganate. Benzoic and formic acids were isolated from the oxidation of 1-methoxy-3-benzylpent-4-ene, and benzoic and methoxypropionic acids from 1-methoxy-5-benzylpent-3-ene. It is seen from the above experiment that the reaction of benzyl magnesium chloride with both of the isomeric methoxychloropentenes forms a similar mixture of isomeric methoxybenzylpentenes. These results lead to the conclusion that both of these reactions occur by means of the same ionic mechanism. Later, the reactions of isomeric methoxychloropentenes with ethyl magnesium bromide were studied. Two products resulted from the action of ethyl magnesium bromide on 1-methoxy-5-chloropent-3-ene: 1-methoxyhept-3-ene in a 55.3% yield and 1-methoxy-6-β-methoxyethyloct-3,7-dien in a 19% yield. These same products, in yields of 63.1% and 22.3% respectively, were obtained from the reaction of ethyl magnesium bromide with 1-methoxy-3-chloropent-4-en. The structure of the products was determined by oxidizing them with potassium permanganate. The glycol, 1-methoxy-hept-3,4-diol was obtained by the oxidation of 1-methoxy-hept-3-en with the calculated amount of potassium permanganate under mild conditions, according to Wagner, and butyric and methoxypropionic acids under more drastic conditions. 1-Methoxy-3,4-dibromoheptane was obtained in 62.2% yield by the addition of bromine to 1-methoxyhept-3-en. Analogous results were obtained by reaction of the isomeric methoxychloropentenes with butyl magnesium bromide. 1-Methoxynon-3-ene in 58.9% yield and 1-methoxy-6-β-methoxyethyloct-3,7-dien in 6.9% yield were obtained from 1-methoxy-5-chloropent-3-en. The same products in similar yields were obtained from the reaction of butyl magnesium bromide with 1-methoxy-3-chloropent-4-en. The

glycol, 1-methoxynon-3,4-diol was obtained by the oxidation of 1-methoxynon-3-en with potassium permanganate and 1-methoxy-3,4-dibromononane by its bromination. The results obtained agreed with those obtained previously in analogous experiments with isomeric ethoxychloropentenes and butoxychloropentenes. Evidently, the stages of the reactions in which 1-methoxyhept-3-en and 1-methoxynon-3-en are formed from both of the isomeric methoxychloropentenes occur by means of an ionic mechanism which is analogous to the one proposed above for the reaction with benzyl magnesium chloride.

The formation of 1-methoxy-6-β-methoxyethyloct-3,7-dien in the reaction of ethyl magnesium bromide and butyl magnesium bromide with the isomeric methoxychloropentenes can be explained by the occurrence of an exchange reaction between them, leading to the formation of the organo-magnesium compound from the methoxychloropentenes, as an intermediate.

$$CH_3OCH_2CH_2CH{=}CHCH_2Cl + C_2H_5MgBr \rightarrow CH_3OCH_2CH_2CH{=}CHCH_2MgBr$$

$$CH_3OCH_2CH_2CH{=}CHCH_2MgBr + ClCH_2CH{=}CHCH_2CH_2OCH_3 \rightarrow CH_3OCH_2CH_2\underset{\displaystyle CH{=}CH_2}{\underset{|}{C}}HCH_2CH{=}CHCH_2CH_2OCH_3$$

1-Methoxy-6-β-methoxyethyloct-3,7-dien was formed as the only product of the direct action of metallic magnesium on the methoxychloropentenes. The structure of 1-methoxy-6-β-methoxyethyloct-3,7-dien was determined by its oxidation with potassium permanganate; formic and methoxypropionic acids were isolated and identified.

The formation of 1-methoxy-6-β-methoxyethyloct-3,7-dien and not 1,10-dimethoxydec-3,7-dien, as could be expected from a normal reaction of a primary methoxychloropentene with magnesium and an organo-magnesium compound, can be explained by means of an abnormal bimolecular mechanism proposed by the authors for an analogous type of reaction in a previous publication [2].

EXPERIMENTAL

Action of benzyl magnesium chloride on 1-methoxy-5-chloropent-3-en. An ether solution of benzyl magnesium chloride was prepared from 8 g of magnesium turnings and 42 g of benzyl chloride in 100 ml of absolute ether. 30 g of 1-methoxy-5-chloropent-3-en was added dropwise to this organo-magnesium compound, and the reaction mixture heated for 5 hours on the water bath. After cooling, it was treated with cold water and dilute hydrochloric acid. The ether layer was separated and dried with calcium chloride; the ether was removed and the residue vacuum distilled. After several redistillations, 8.9 g of 1-methoxy-3-benzylpent-4-ene, b.p. 111-113° at 11 mm, was obtained.

n_D^{20} 1.4860; d_4^{20} 0.9145; MR_D 59.65; calculated 59.81.

0.1216 g substance: 0.3647 g CO_2; 0.1017 g H_2O. Found %: C 81.85; H 9.36. $C_{13}H_{18}O$. Calculated %: C 82.00; H 9.47.

16.7 g of 1-methoxy-5-benzylpent-3-en, b.p. 123-124.5° at 10 mm, was also obtained.

n_D^{20} 1.5045; d_4^{20} 0.9336; MR_D 60.31; calculated 59.81.

0.1065 g substance: 0.3193 g CO_2; 0.0908 g H_2O. Found %: C 81.82; H 9.54. $C_{13}H_{18}O$. Calculated %: C 82.10; H 9.47.

In addition to the above, 6.3 g of dibenzyl, b.p. 132° at 100 mm, m.p. 52° was obtained.

Action of benzyl magnesium chloride on 1-methoxy-3-chloropent-4-en. An ether solution of benzyl magnesium chloride was prepared from 9.4 g of magnesium turnings and 53 g of benzyl chloride in 100 ml of absolute ether. 30 g of 1-methoxy-3-chloropent-4-en was slowly added dropwise to this solution, and the reaction mixture was then heated for 4 hours on a water bath. The reaction mixture was processed in the same manner as in the previous experiment. After several redistillations in vacuum the following were obtained: 7.6 g of 1-methoxy-3-benzylpent-4-en, b.p. 114-115° at 13 mm, n_D^{20} 1.4855; d_4^{20} 0.9153, 14.1 g 1-methoxy-5-benzylpent-3-en, b.p. 135-136° at 18 mm, n_D^{20} 1.5065, d_4^{20} 0.9346; and 8.1 g of dibenzyl, m.p. 51.5°.

Oxidation of 1-methoxy-5-benzylpent-3-ene with potassium permanganate. 45 g of potassium permanganate was added in portions with continuous stirring over a 4 hour period to 8 g of 1-methoxy-5-benzylpent-3-en in 350 ml of distilled water. The manganese dioxide precipitate was filtered and washed three times with hot distilled water. The aqueous solution of the salts was evaporated to a volume of 60 ml, and treated with dilute hydrochloric acid. The solution was extracted several times with ether and the ether extracts dried over $CaCl_2$. After removal of the ether, the residue was vacuum distilled. Three fractions were obtained (at 12 mm): 1) 106-113°, 1.9 g; 2) 114-140°, 0.5 g; 3) 140-146°, 2.5 g.

When the first fraction was redistilled, 1.1 g of methoxypropionic acid, b.p. 108-110° at 12 mm, n_D^{20} 1.4189 was isolated.

The third fraction solidified into a crystalline mass. Crystals of benzoic acid, m.p. 120-121°, were obtained on recrystallization from water.

Oxidation of 1-methoxy-3-benzylpent-4-en with potassium permanganate. 50 g of potassium permanganate was slowly added with thorough shaking to a flask containing 9 g of 1-methoxy-3-benzylpent-4-en. After decolorization of the liquid, the manganese dioxide was filtered and washed with hot distilled water. The water solution of the salts was evaporated to a volume of 65-70 ml, the salts decomposed with phosphoric acid, and the solution extracted four times with ether. The ether solution was dried with calcium chloride, the ether removed, and the residue distilled. Formic acid, b.p. 101-105°, n_D^{20} 1.3780; d_4^{20} 1.2210, was isolated; it had the sharp characteristic odor. A black precipitate of silver was obtained with a solution of ammoniacal silver oxide (on heating). After removal of the formic acid, the distillation flask was cooled. The crystalline mass which formed was recrystallized from water. White crystals of benzoic acid, m.p. 121°, were isolated.

Action of ethyl magnesium bromide on 1-methoxy-5-chloropent-3-en. 7.5 g of magnesium turnings were placed in a round-bottomed flask equipped with a reflux condenser and a dropping funnel. The magnesium turnings were activated by heating with a crystal of iodine, and on cooling, were covered with absolute ether. A solution of 35 g of ethyl bromide in 100 ml of absolute ether was then slowly added dropwise. The reaction mixture was heated for 1 hour on the water bath. 30 g of 1-methoxy-5-chloropent-3-en was then added dropwise to the organomagnesium compound, and the reaction mixture was heated for 2 hours on the water bath. At the end of the reaction, the mixture was treated with cold water and dilute hydrochloric acid. The ether layer was separated in a separatory funnel and dried over calcium chloride. After removal of the ether on the water bath, the residue was vacuum distilled. 3 fractions were obtained: 1) 53-60° at 30 mm, n_D^{20} 1.4198; 16.5 g; 2) 61-121° at 30 mm; n_D^{20} 1.4368; 1.1 g; 3) 113-118° at 16 mm; n_D^{20} 1.450; 4.8 g. 15.8 g of 1-methoxyhept-3-en, b.p. 58-59° at 30 mm, was obtained by redistilling the first fraction.

n_D^{20} 1.4200; d_4^{20} 0.8079; MR_D 40.09; calculated 40.32.

0.1106 g substance; 0.3030 g CO_2; 0.1243 g H_2O. Found %: C 74.76; H 12.58. $C_8H_{16}O$. Calculated %: C 75.00; H 12.50.

4.2 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien, b.p. 113-114° at 13 mm, was obtained by redistilling the third fraction.

n_D^{20} 1.4510; d_4^{20} 0.8846; MR_D 60.28; calculated 59.97.

0.1123 g substance: 0.2983 g CO_2; 0.1104 g H_2O. Found %: C 72.49; H 11.00. $C_{12}H_{22}O_2$. Calculated %: C 72.72; H 11.11.

Action of ethyl magnesium bromide on 1-methoxy-3-chloropent-4-en. An ether solution of ethyl magnesium bromide was prepared from 9.1 g magnesium turnings and 43.1 g of ethyl bromide. 40 g of 1-methoxy-3-chloropent-4-en was then added dropwise to it, and the reaction mixture was heated for 1 hour on the water bath. The jelly-like mass which formed was treated with cold water and a cold solution of dilute hydrochloric acid. The ether layer was dried with calcium chloride, the ether was removed, and the residue vacuum distilled. After several redistillations, 23.5 g of 1-methoxyhept-3-en, b.p. 60-61° at 35 mm, n_D^{20} 1.4204; d_4^{20} 0.8080, and 6.7 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien, b.p. 106-108° at 9 mm, n_D^{20} 1.4500; d_4^{20} 0.8850, were isolated.

Oxidation of 1-methoxyhept-3-en with potassium permanganate to the glycol. 100 ml of distilled water and 15 g of 1-methoxyhept-3-en were placed in a 5 liter flask. A weakly basic solution of 25 g of potassium permanganate in 2500 ml of water was slowly added dropwise with efficient mechanical stirring to the reaction mixture. The addition took 10 hours and the reaction mixture was then allowed to stand overnight. After the decolorization of the liquid, the manganese dioxide was filtered and washed several times with hot water. The filtrate was evaporated in vacuum to a volume of 40-50 ml, treated with hydrochloric acid, and extracted with ether. The ether extract was dried over sodium sulfate, the ether removed, and the residue vacuum distilled. 4.1 g of 1-methoxyhept-3,4-diol, b.p. 116-120° at 10 mm, resulted from the distillation.

n_D^{20} 1.4460; d_4^{20} 0.9950; MR_D 43.42; calculated 43.84.

0.1113 g substance: 0.2406 g CO_2; 0.1096 g H_2O. Found %: C 58.99; H 11.02. $C_8H_{16}O_3$. Calculated %: C 59.25; H 11.11.

Oxidation of 1-methoxyhept-3-en with potassium permanganate to the acids. 10.5 g of 1-methoxyhept-3-en and 540 ml of water were placed in a one-liter flask. 30 g of potassium permanganate was slowly added with constant shaking, and the flask with the reaction mixture was left at room temperature for 12 hours. The manganese dioxide precipitate was filtered and washed several times with hot water. The filtrate was evaporated, in vacuum, to a volume of 50-60 ml, treated with hydrochloric acid, and extracted with ether. The ether extract was dried over calcium chloride, the ether removed, and the residue vacuum distilled. On distillation, 2.1 g of butyric acid, b.p. 160-162°, n_D^{20} 1.400; d_4^{20} 0.9680, and 2.5 g of methoxypropionic acid, b.p. 106-107° at 100 mm, n_D^{20} 1.4168, were obtained. (According to the literature methoxypropionic acid has a b.p. of 107-108° at 12 mm; n_D^{20} 1.4178).

Action of bromine on 1-methoxyhept-3-en. 10 g of bromine was added, with efficient stirring and cooling, (-15 to -18°) to 8 g of 1-methoxyhept-3-en. Upon distillation of the reaction mixture 11.2 g of 1-methoxy-3,4-dibromoheptane, b.p. 116-119° at 16 mm, was obtained.

n_D^{20} 1.4960; d_4^{20} 1.5055; MR_D 56.00; calculated 56.23.

0.1116 g substance: 0.1449 g AgBr. Found %: Br 55.20. $C_8H_{16}OBr_2$. Calculated %: Br 55.49.

Action of butyl magnesium bromide on 1-methoxy-5-chloropent-3-en. An ether solution of butyl magnesium bromide was prepared from 6.5 g of magnesium turnings and 38.7 g of butyl bromide. 30 g of 1-methoxy-5-chloropent-3-en was slowly added, dropwise with cooling, to it, and the reaction mixture was then heated for 3 hours on the water bath. At the end of the reaction, it was treated with water and dilute hydrochloric acid. After drying and removing the ether, the reaction mixture was twice vacuum distilled; 20.6 g of 1-methoxynon-3-en, b.p. 68-69° at 9 mm, was isolated.

d_4^{20} 0.8082; n_D^{20} 1.4295; MR_D 49.81; calculated 49.56.

0.1099 g substance; 0.3092 g CO_2; 0.1247 g H_2O. Found %: C 76.78; H 12.70. $C_{10}H_{20}O$. Calculated %: C 76.92; H 12.82.

2 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien, b.p. 114-116° at 15 mm, n_D^{20} 1.4515; d_4^{20} 0.8841, was also obtained.

Action of butyl magnesium bromide on 1-methoxy-3-chloropent-4-en. An ether solution of butyl magnesium bromide was prepared from 10.3 g of magnesium turnings and 61.3 g of butyl bromide. 50 g of 1-methoxy-3-chloropent-4-en was added dropwise to the above solution. The reaction mixture was then heated for 2 hours on the water bath. The reaction mixture was then processed in a manner analogous to the previous experiment. Upon distillation of the reaction products 32.1 g of 1-methoxynon-3-en, b.p. 71-72° at 12 mm, n_D^{20} 1.4298; d_4^{20} 0.8075, and 6.1 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien, b.p. 113-114° at 12 mm, n_D^{20} 1.4512; d_4^{20} 0.8840, was obtained.

Oxidation of 1-methoxynon-3-en with potassium permanganate to the glycol. 15 g of 1-methoxynon-3-en and 100 ml of distilled water were placed in a 2-liter flask. A weakly basic solution of 10.1 g of potassium permanganate in 1000 ml of water was then slowly added with efficient shaking. The addition took 6 hours. The reaction mixture was allowed to stand for 16 hours at room temperature. The manganese dioxide precipitate was filtered and washed with hot distilled water. The filtrate was evaporated to a volume of 50-60 ml, treated with dilute hydrochloric acid, and extracted with ether. The ether extract was dried over sodium sulfate, the ether removed, and the residue vacuum distilled. 3.1 g of 1-methoxynon-3,4-diol, b.p. 142-144° at 13 mm, was isolated.

n_D^{20} 1.4442; d_4^{20} 0.9782; MR_D 53.29; calculated 53.07.

0.1199 g substance: 0.2762 g CO_2; 0.1224 g H_2O. Found %: C 62.87; H 11.42. $C_{10}H_{22}O_3$. Calculated %: C 63.15; H 11.58.

Action of bromine on 1-methoxynon-3-en. 8.2 g of bromine was slowly added dropwise with cooling and stirring to 8 g of 1-methoxynon-3-en. The reaction product was distilled. 8.9 g of 1-methoxy-3,4-dibromopropane, b.p. 137-139° at 11 mm was isolated.

n_D^{20} 1.4920; d_4^{20} 1.4033; MR_D 65.32; calculated 65.47.

0.1165 g substance: 0.1379 g AgBr. Found %: Br 50.36. $C_{10}H_{20}OBr_2$. Calculated %: Br 50.50.

Action of magnesium on 1-methoxy-5-chloropent-3-en. 2.4 g of magnesium turnings were placed into a flask containing a stirrer, dropping funnel, and reflux condenser. The magnesium turnings were activated by heating with a crystal of iodine, and on cooling, were covered with absolute ether. A few drops of ethylbromide were then added followed by the slow dropwise addition of 30 g of 1-methoxy-5-chloropent-3-en. The reaction mixture was then heated for 5 hours with constant stirring. At the end of the reaction it was diluted with water,

and the ether layer separated and dried over calcium chloride. The ether was removed on the water bath and the residue vacuum distilled. On distillation, 15.7 g of 1-methoxy-5-chloropent-3-en was recovered, and 6.7 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien, b.p. 111-112 at 10 mm, n_D^{20} 1.4515; d_4^{20} 0.8865, was isolated.

Action of magnesium on 1-methoxy-3-chloropent-4-en. An ether solution of 30 g of 1-methoxy-3-chloropent-4-en was added, dropwise, to 2.4 g of activated magnesium covered by a layer of absolute ether. The reaction mixture was then processed in the same way as the previous experiment. On distillation, 17.8 g of 1-methoxy-3-chloropent-4-en was recovered and 5.5 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien b.p. 110-112° at 10 mm, n_D^{20} 1.4518; d_4^{20} 0.8855, was isolated.

Oxidation of 1-methoxy-6-β-methoxyethyloct-3,7-dien with potassium permanganate. 39.5 g of pulverized potassium permanganate was added, in small portions, with continuous stirring, to 15.5 g of 1-methoxy-6-β-methoxyethyloct-3,7-dien in 800 ml of distilled water in a 2 liter flask. After decolorization of the liquid, the manganese dioxide precipitate was filtered and washed several times with hot water. The filtrate was evaporated, treated with phosphoric acid, and extracted with ether. After removal of the ether, the residue was distilled. Formic acid, b.p. 101-106°, n_D^{20} 1.3770, sharp characteristic odor, was isolated. A black precipitate was formed (on heating) with an ammoniacal silver oxide solution. Methoxypropionic acid, b.p. 107-109° at 11 mm, n_D^{20} 1.4173, and a thick liquid fraction, b.p. 190-210° at 9 mm, were also obtained.

SUMMARY

1. The reactions of the isomeric methoxychloropentenes with benzyl magnesium chloride, ethyl magnesium bromide, and butyl magnesium bromide was studied.

2. Mixtures of isomeric methoxybenzylpentenes, identical in composition, were formed as a result of the reaction of benzyl magnesium chloride on the isomeric methoxychloropentenes.

3. Mixtures of the corresponding 1-methoxy-5-alkylpent-3-enes and 1-methoxy-6-β-methoxyethyloct-3,7-dien were obtained as a result of the action of ethyl magnesium bromide and butyl magnesium bromide on the isomeric methoxychloropentenes. The second compound was also obtained by the direct action of magnesium on the isomeric methoxychloropentenes.

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ALLYLIC REARRANGEMENTS

XVIII. REACTION OF ISOMERIC METHOXYCHLOROPENTENES WITH SALTS OF XANTHOGENIC ACIDS

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In a series of previous communications on the study of allylic rearrangements, the reactions of isomeric alkoxychloropentenes with various reagents was studied: alcoholic alkali, alkali metal acetates and alcoholates, sodium hydrosulfide, amines, sodio malonic ester, dialkyl phosphates, and organo-magnesium compounds. It was shown that with all of these, the reaction proceeds mainly according to two mechanisms – the bimolecular and the monomolecular. The reaction by means of the bimolecular mechanism has only one stage, is without rearrangements, and leads to compounds with structures analogous to the starting material. The reaction by means of the bimolecular mechanism has two stages; it proceeds by means of the initial formation of a carbonium ion and leads to the formation of either mixtures of isomeric compounds, or just one. In certain cases, a third mechanism is possible for the reaction – an abnormal bimolecular mechanism. This is of secondary importance as compared to the other two. The primary allylic chlorides, in comparison with the secondary, have a much more pronounced tendency to react by means of the bimolecular mechanism, which is related to peculiarities in their structure.

In order to further develop and increase the number of examples of reactions accompanied by allylic rearrangements, the preparation of xanthogenic esters from allylic halides was studied in this investigation.

The reaction between allylic halides and xanthogenic salts has remained almost uninvestigated up to now. Only allyl xanthogenates, obtained by the reaction of allyl bromide with xanthogenic salts [1], are reported in the literature; however, these publications do not give any bases for discussing the possibility of the occurrence of allylic rearrangements during these reactions. The study of the reaction of isomeric allylic halides with xanthogenic salts is also of considerable interest for gathering data to further develop the xanthogenic method of Chugaev for the preparation of unsaturated compounds.

The reactions of isomeric methoxychloropentenes with sodium ethyl- and butyl-xanthogenates was studied. The reaction was effected by heating in alcoholic solutions. Methoxypentenyl ethylxanthogenate and a series of lower boiling fractions were obtained in the experiments with primary methoxychloropentenes and sodium ethylxanthogenate.

$$CH_3OCH_2CH_2CH{=}CHCH_2Cl + C_2H_5OCSS^- \rightarrow CH_3OCH_2CH_2CH{=}CHCH_2SSCOC_2H_5 + Cl^-.$$

It is interesting to point out that methoxypentenyl ethylxanthogenate is obtained in pure form only when equimolecular or smaller amounts of sodium ethylxanthogenate than methoxychloropentene are used. When an excess of the sodium xanthogenate is used, a fraction is formed which has the same boiling point as methoxypentenyl ethylxanthogenate, but with much lower values for the constants and a much lower sulfur content. This occurrence, which seemed very strange at first, was explained when the reaction between sodium ethylxanthogenate and a secondary methoxychloropentene, 1-methoxy-3-chloropent-4-en, was studied. Dimethoxypentenyl thioether $(CH_3OCH_2CH_2CH{=}CHCH_2)_2S$ was obtained as the main product along with a series of lower boiling products.

The thioether, according to its constants, corresponded closely to the one obtained by one of the authors and N. N. Kudryavtseva, by the action of sodium hydrosulfide on the isomeric methoxychloropentenes [2]. It was shown that the primary methoxypentenyl mercaptan, formed from both of the isomeric methoxychloropentenes as main products, was transformed, under these reaction conditions (heating in alcohol), into the corresponding thioether by the elimination of a molecule of hydrogen sulfide. According to the constants, both of the isomeric methoxychloropentenes formed the identical thioether. The structure of the mercaptan and the thioethers was determined by oxidizing them with potassium permanganate.

The formation of methoxypentenyl thioether, by the reaction of secondary methoxychloropentenes with sodium ethylxanthogenate can be explained in the following manner: the secondary methoxychloropentene reacts monomolecularly with sodium ethylxanthogenate, in the first stage of the reaction, with complete allylic rearrangement to form methoxypentenyl ethylxanthogenate; however, this reaction occurs at a considerably slower rate in comparison to the analogous reaction of the methoxychloropentene, because its rate is limited by the slow formation of ions from the secondary methoxychloropentene by the action of the solvent; as a result, the methoxypentenyl ester which has already been formed, is in contact, for long periods of time with the yet unreacted xanthogenate and evidently, with the sodium ethylate present in the medium, and decomposes to form the mercaptan [1]; the latter, under these reaction conditions (heating in alcohol) is transformed, as shown previously [2], into the thioether by the elimination of hydrogen sulfide.

The abnormal behavior of the secondary methoxychloropentene in this reaction is not unusual, as this behavior was noted frequently in other reactions. For example, when it was reacted with sodio alkylacetoacetic ester, the methoxypentenyl alkyl acetoacetic ester formed in the first stage of the reaction is decomposed by the action of the alcoholate and the sodio alkyl acetoacetic ester into disubstituted derivatives of acetic acid [3]; on reaction with dialkyl phosphate salts, an addition of a second molecule of sodium dialkylphosphate occurs at the double bond of the methoxypentenyl phosphoric ester formed in the first stage of the reaction [4].

In the light of the many reactions with secondary methoxychloropentenes conducted for determination of the reaction mechanism the results obtained from the reaction of primary methoxychloropentenes with xanthogenates, which seem so strange at first, become quite understandable. As was previously mentioned, methoxypentenyl ethylxanthogenate can only be obtained in pure form in the absence of an excess of the sodium xanthogenate in the reaction medium. In the presence of the latter, a complete decomposition of the ester to methoxypentenylmercaptan followed by its transformation to the thioether occurs. The boiling points of methoxypentenyl ethylxanthogenate and methoxypentenyl ether are so close that they cannot be separated by distillation; they can be distinguished by differences in the refractive indices, densities and especially by the sulfur content, which differs considerably. The variation of the constants and the amount of sulfur in the main fractions of the xanthogenic ester obtained in the series of experiments with excesses of the xanthogenate, can be explained by the presence of distinguishable amounts of thioether. Results analogous to those reported above for the reaction with ethylxanthogenate were obtained for the reaction between the isomeric methoxychloropentenes and sodium butylxanthogenate. Methoxypentenyl butylxanthogenate resulted from the action of sodium butylxanthogenate on 1-methoxy-5-chloropent-3-en, and dimethoxypentenyl thioether from the analogous reaction with 1-methoxy-3-chloropent-4-en.

EXPERIMENTAL

Action of sodium ethylxanthogenate on 1-methoxy-5-chloropent-3-en. 23 g of carbon disulfide was slowly added, dropwise with cooling, to a solution of sodium ethylate prepared from 6.3 g of metallic sodium and 100 ml absolute ethanol. 40 g of 1-methoxy-5-chloropent-3-en was then added, in the cold, to the alcoholic solution of sodium ethylxanthogenate. Very rapid precipitation of sodium chloride occurred. The reaction mixture was heated for 2 hours on the water bath. After filtration of the sodium chloride precipitate and removal of the alcohol, the residue was vacuum distilled. After two distillations, in addition to fractions boiling at 66-124° at 10 mm, 23.3 g of methoxypentenyl ethylxanthogenate, b.p. 161-162 at 12 mm, was isolated.

n_D^{20} 1.5315; d_4^{20} 1.0676.

0.7181 g substance: 0.3684 g $BaSO_4$. Found %: S 29.08. $C_8H_{16}O_2S_2$. Calculated %: S 29.09.

Action of sodium butylxanthogenate on 1-methoxy-5-chloropent-3-en. An alcoholic solution of sodium butylxanthogenate was prepared from 16 g of carbon disulfide, 3.2 g of sodium, and 80 ml of absolute butyl alcohol. 20 g of 1-methoxy-5-chloropent-3-en was then slowly added dropwise to the alcoholic solution of the sodium xanthogenate. A very rapid precipitation of sodium chloride occurred. After the addition of the chloride, the reaction mixture was heated for 2 hours on the water bath. The sodium chloride precipitate was filtered, the butyl alcohol was removed in a slight vacuum, and the residue was vacuum distilled. 18.9 g of methoxypentenyl butylxanthogenate, b.p. 170-170.8° at 10 mm, was obtained.

n_D^{20} 1.5220; d_4^{20} 1.0400.

0.1286 g substance; 0.2402 g $BaSO_4$ Found %: S 25.66. $C_{11}H_{20}O_2S_2$. Calculated %: S 25.72.

Action of sodium ethylxanthogenate on 1-methoxy-3-chloropent-4-en. 14.3 g of carbon disulfide was slowly added, dropwise, with ice cooling, to a solution of sodium ethylate prepared from 3.9 g of metallic sodium and 50 ml of absolute ethyl alcohol. 20 g of 1-methoxy-3-chloropent-4-en was then added, and the reaction mixture was heated for two hours on the water bath. The sodium chloride precipitated much more slowly than during the analogous reaction with 1-methoxy-5-chloropent-3-en.

At the end of the heating, the sodium chloride precipitate was filtered, the ethyl alcohol was removed on the water bath, and the residue was vacuum distilled. After two distillations, in addition to fractions boiling at 84-144° at 10 mm; 5.24 g of di-methoxypentenyl thioether, b.p. 161-163° at 11 mm, was obtained.

n_D^{20} 1.4943; d_4^{20} 0.9786.

0.1272 g substance: 0.1458 g $BaSO_4$. Found %: S 14.01. $C_{12}H_{22}O_2S$. Calculated %: S 13.90.

Action of sodium butylxanthogenate on 1-methoxy-3-chloropent-4-en. A solution of sodium butylate in absolute butyl alcohol was prepared from 6.9 g of metallic sodium and 200 ml of butyl alcohol. 28 g of carbon disulfide was then added, dropwise with cooling, followed by 40 g of 1-methoxy-3-chloropent-4-en. The reaction mixture was heated for 3 hours on the water bath. After separation of the sodium chloride and removal of the butyl alcohol, the residue was vacuum distilled. After two distillations, 15.9 g of dimethoxypentenyl thioether, b.p. 157-159° at 8 mm, n_D^{20} 1.4935; d_4^{20} 0.9758, and a series of lower boiling fractions were obtained.

SUMMARY

1. The reaction between the isomeric methoxychloropentenes and sodium ethyl and butylxanthogenate was studied.

2. 1-Methoxy-5-chloropent-3-en reacted normally with sodium ethyl- and butylxanthogenate to form 1-methoxypentenyl ethyl- and butylxanthogenate.

3. Dimethoxypentenyl thioether was formed as the main product of the reaction between sodium ethyl- and butylxanthogenate with 1-methoxy-3-chloropent-4-en. The reaction occurred with a complete allylic rearrangement. A mechanism for the formation of dimethoxypentenyl thioether is given.

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A STUDY OF THE TRANSFORMATIONS OF PINACONES WITH SUBSTITUTED ACETYLENIC RADICALS

IX. SYNTHESIS AND TRANSFORMATIONS OF TRIPHENYLPHENYL-ACETYLENYL ETHYLENE GLYCOL (1,1,2,4-TETRAPHENYLBUTYN-3-DIOL-1,2)

E. D. Venus-Danilova and V. I. Serkova

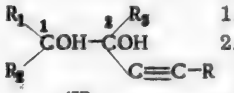
In a previous communication [1] the transformations of trimethylphenylacetylenylethylene glycol (2,3-dimethyl-5-phenylpentyne-4-diol-2,3) by the action of 30% sulfuric acid were discussed.

An acetylenic ketone, dimethylphenylacetylenylacetylmethane, as well as the decomposition products of an ethylenic γ-ketol, a dienic ketone and a mixture of ethylideneacetophenone and acetone, were found in the transformation products of this glycol.

The formation of these products shows that trimethylphenylacetylenylethylene glycol undergoes both a pinacoline and an acetylene-allene rearrangement at the same time, similar to the previously studied compounds, symmetrical methyldiphenylphenylacetylenylethylene glycol [2], methyldiphenyltertiarybutylacetylenylethylene glycol [3], and trimethylphenylacetylenyl glycol [1].

In order to continue the study of the effects of the substituents of the hydroxyl-containing carbon atoms of the acetylenic tertiary γ-glycols [4,5,6,7,1,2,3] on their transformations, as well as to elucidate the mechanism [8] of this transformation and to study the properties of ethylenic γ-ketols, the eighth member of this series, triphenylphenylacetylenylethylene glycol (1,1,2,4-tetraphenylbutyn-3-diol-1,2) [1] was synthesized and subjected to the action of sulfuric acid under the previously described conditions.

From the previous study it was concluded that the presence of two phenyl groups on the first hydroxyl-containing carbon atom of the glycol (II) favors the pinacoline rearrangement; a methyl group on the second hydroxyl-group-containing atom has the analogous effect.



(II)

1. Pinacoline rearrangement (dehydration) $R_1 = R_2 = C_6H_5$, $R_3 = CH_3$
2. Acetylene-allene rearrangement (isomerization) $R_1 = R_2 = CH_3$, $R_3 = C_6H_5$

The opposite arrangement of the groups, the methyl groups on the first carbon atom and the phenyl groups on the second, favors the acetylene-allene rearrangement.

The structure of the triphenylphenylacetylenylethylene glycol is such that both transformations are probable: 1) the pinacoline rearrangement because of the presence of the phenyl groups on the first carbon atom, and 2) the acetylene-allene rearrangement, because of the phenyl group on the second carbon atom of the glycol.

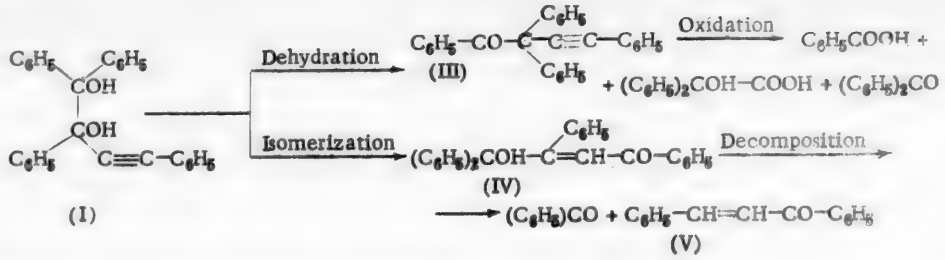
The experimental results proved this hypothesis to be true.

Triphenylphenylacetylenylethylene glycol (I) was obtained as coarse crystals, m.p. 114-115°, by the action of phenylbenzoin upon phenylacetylenyl magnesium bromide (Iotsich method) in a 53% yield based on the quantity of phenylbenzoin used.

As a result of the action of 30% sulfuric acid on triphenylphenylacetylenylethylene glycol, two products were isolated: a crystalline substance, m.p. 186-187°, and an oily liquid.

Upon the oxidation of the crystalline substance, benzoin, benzilic acid, and benzophenone were obtained. The structure of the ketone obtained, is, therefore, diphenylphenylacetylenylbenzoylmethane (1,2,2,4-tetraphenylbutyne-3-one-1)(III). In this case the ketone is formed by the removal of the mobile hydroxyl group in the α-position

to the triple bond [1,2,3,7].



A study of the oily liquid showed that the substance contained a double bond and a carbonyl group. A distillation at reduced pressure did not produce any homogeneous substance with a narrow boiling point. This fraction was shown to be a mixture of benzophenone and benzalacetophenone (V) by a molecular weight determination and by an oxidation of the substance. The above was confirmed by the formation of semicarbazones and by the pyrazoline reaction.

Benzophenone and benzalacetophenone, apparently, result from a ketonic cleavage of the extremely unstable ethylenic γ-ketol [1,1,2,4-tetraphenylbutyne-2-ol-1-one-4) [IV] which probably decomposed before distillation either by the action of the sulfuric acid or on washing the ether solution with the dilute aqueous sodium carbonate.

This conclusion was verified by the decreased molecular weight of the oily liquid and by its oxidation products (benzoic acid, benzoylformic acid, and benzophenone) before vacuum distillation. The instability of ethylenic γ-ketols of analogous structure and their ketonic cleavage was discovered previously [1,2].

On heating triphenylphenylacetylenylethylene glycol with 35% sulfuric acid, a slight fluorescence was detected in the acidic solution, which indicated that a small amount of an oxonium salt of a substituted dihydrofuran was present. However, after the separation of the transformation products of the glycol – the acetylenic ketone, benzalacetophenone, and benzophenone – only traces of a crystalline substance giving a fluorescence in strong sulfuric acid were isolated by ether extraction. This substance was not investigated further because of the small amount isolated.

Therefore, triphenylphenylacetylenylethylene glycol, on treatment with 30 and 35% sulfuric acid, forms the products of the pinacoline and the acetylene-allene rearrangements. The acetylenic ketone is obtained from the dehydration of the glycol and, on isomerization, the glycol forms the unstable ethylenic γ-ketol which splits, as soon as it is formed, into benzophenone, and benzalacetophenone.

EXPERIMENTAL

L. The Synthesis of Triphenylphenylacetylenylethylene Glycol (1,1,2,4-Tetraphenylbutyne-3 Diol-1,2).

An ether solution of 7.6 g of phenylacetylene was added to a freshly prepared solution of ethyl magnesium bromide made from 1.8 g of magnesium and 8 g of ethyl bromide. The reaction mixture was heated slightly on the water bath until the evolution of ethane ceased.

A solution of 10 g of phenylbenzoin (m.p. 86-87°) was added to the above Grignard with stirring and cooling with ice. After the addition of all of the phenylbenzophenone, the contents of the flask were heated to a slight reflux of the ether.

After three days the reaction mixture was decomposed with ice and water, acidified with dilute sulfuric acid, and extracted with ether. The ether extracts were washed with aqueous sodium carbonate, then with water, and dried with fused sodium sulfate. After the removal of the ether, the thick residual mass quickly began to crystallize. After recrystallization from a mixture of petroleum ether and ether, 8.5 g of a substance, coarse crystals, m.p. 114-115°, was obtained. The yield was 74% of the theoretical, calculated on the amount of phenylbenzoin used.

Three runs using this synthesis produced 28.8 g of the glycol with an average yield of 61% of the theoretical.

0.1096 g substance; 0.3449 g CO_2; 0.0587 g H_2O. 0.1322 g substance: 0.4159 g CO_2; 0.0678 g H_2O. Found %: C 85.82, 85.80; H 5.95, 5.69. $C_{28}H_{22}O_2$. Calculated %: C 86.15; H 5.67. 0.2216 g substance; 20.50 g C_6H_6: Δt 0.14°. Found: M 386. $C_{28}H_{22}O_2$. Calculated M: 390.

The number of hydroxyl groups was determined according to Terentyev.

0.0695 g substance: 8.2 ml CH_4 (14°, 751.5 mm). Found v_0 7.6 ml; % OH 7.9. $C_{28}H_{24}(OH)_2$. Calculated v_0 8.5 ml; % OH 8.7.

II. The Action of Sulfuric Acid on Triphenylphenylacetylenylethylene Glycol.

Expt. 1. The action of 30% sulfuric acid. 8 g of the glycol, m.p. 114-115°, was heated with 80 ml of 30% sulfuric acid to a gentle boil for 3 hours with good stirring. The glycol melted and formed a yellow mass; no fluorescence could be observed in the solution. The ether extract of the acidic solution was washed with aqueous sodium carbonate and then with water. After the removal of the ether, 7.3 g of a thick, light-yellow liquid which upon standing gave 0.8 g of a crystalline substance, m.p. 185-187°, was obtained. After recrystallization from a boiling mixture of ether and petroleum ether, the crystals melted at 186-187°.

The liquid from which the crystalline substance separated, was unsaturated in character (tests with aqueous potassium permanganate and bromine in chloroform).

Nothing could be isolated from the ether extracts of the neutralized solution.

Expt. 2. The action of 35% sulfuric acid. 7 g of the glycol was mixed with ten parts by weight of 35% sulfuric acid and the solution boiled gently for three hours.

On cooling, a thick, sticky, dark-brown liquid layer containing dispersed crystals separated. The lower aqueous acidic layer had a barely detectable, greenish-yellow fluorescence.

6.2 g of a thick yellow liquid, from which 0.5 g of crystals, m.p. 185-187° (analogous to those obtained in the first experiment) separated on standing, was obtained from the ether extracts.

The ether extracts of the neutralized solution (the fluorescence disappeared when the solution was neutralized with aqueous sodium carbonate) gave an insignificant amount of a solid substance showing a fluorescence in strong sulfuric acid. The substance was not investigated further because of its small quantity.

III. The Substance With M.P. of 186-187° Obtained from the Acidic Solution.

The substance is soluble in benzene and pyridine, and slightly in ether. It does not give methane with methyl magnesium iodide. It decolorizes a solution of bromine in chloroform and aqueous potassium permanganate.

0.0966 g substance: 0.3187 g CO_2; 0.0460 g H_2O. 0.0800 g substance: 0.2641 g CO_2; 0.0374 g H_2O. Found %: C 89.98, 90.04; H 5.29, 5.19. $C_{28}H_{20}O$. Calculated %: C 90.32; H 5.37. 0.2230 g substance; 31.0 g C_6H_6: Δt 0.10°. Found: M 359. $C_{28}H_{20}O$. Calculated: M 372.

From these results it can be concluded that this substance is an acetylenic ketone obtained by the dehydration of triphenylphenylacetylenylethylene glycol. However, as with the previously studied phenylphenylacetylenylbenzoylmethane [7], the semicarbazone could not be obtained. The yield of the ketone was 0.8 g, 10.5% of the theoretical.

In order to establish the structure of the ketone, it was oxidized with potassium permanganate in pyridine.

Oxidation of the ketone with m.p. of 186-187°. For the oxidation 1 g of the ketone dissolved in 50 ml of pyridine, and 50 ml of 2% aqueous potassium permanganate were used. The last 0.6 g of the potassium permanganate was added in small portions to correspond with the decolorization of the solution. The oxidation was run over a five hour period, at first, in the cold, and at the end heated to 40°. After decolorization of the solution, the manganese dioxide was filtered off and washed with hot water. Pyridine and other steam-volatile substances were removed from the filtrate by heating it in a slight vacuum. The pyridine in the distillate was neutralized with the calculated amount of sulfuric acid and an ether extraction was made. Benzophenone was obtained from the ether extracts and characterized by its melting point and by its semicarbazone, m.p. 164°, which gave no depression in melting point when mixed with authentic benzophenone semicarbazone. Benzophenone was also separated from the neutral steam-distillable products.

Dilute sulfuric acid was used to liberate the acids from the concentrated solution of their salts after the neutral substances were steam-distilled. A copious amount of benzoic acid, m.p. 120°, separated. After separation of the benzoic acid, the filtrate was extracted with ether to give a small amount of a crystalline substance which gave a red color characteristic for benzilic acid [9] with strong sulfuric acid. No other acids could be found in the oxidation products of the ketone.

Therefore, on the basis of the oxidation products—benzoic acid, benzilic acid, and benzophenone (a

product of the further oxidation of benzilic acid), the structure diphenylphenylacetylenylbenzoylmethane [1,2,2,4-tetraphenylbutyne-3-one-1) [III] can be assigned to the ketone obtained.

IV. Investigation of the Liquid From the Acidic Solution.

The liquid readily decolorizes aqueous potassium permanganate and bromine water. It does not give a qualitative test for the presence of a hydroxyl group. It forms a semicarbazone, m.p. 156-159°. It reacts with phenylhydrazine to form a polycrystalline mass which shows a strong pyrazoline reaction.

When the substance was vacuum distilled at 3 mm, a fraction, b.p. 130-145°, was obtained. A molecular-weight determination and an oxidation of this substance showed that it was not homogeneous.

0.1340 g substance; 16.96 g C_6H_6; Δt 0.23°. Found: M 174. $C_{13}H_{10}O$ (benzophenone). Calculated: M 182. $C_{15}H_{12}O$ (benzalacetophenone). Calculated: M 208. $C_{28}H_{22}O_2$ (ethylidene γ-ketol). Calculated: M 390.

Oxidation of the fraction with b.p. 130-145°, at 3 mm.

50 ml of a 2% aqueous solution of potassium permanganate was added to a solution of 1 g of the liquid in 20 ml of pyridine. The remaining 1 g of the oxidizing agent was added in small portions to correspond with the decolorization of the solution. The oxidation was conducted at 30-35° for a 3-hour period with thorough mixing.

After removal of the pyridine in the usual manner, benzophenone, m.p. 47°, giving a semicarbazone with m.p. 164° was isolated from the neutral products. Benzoic acid, m.p. 120°, was obtained by the splitting of the salts of the organic acids. After the removal of the benzoic acid, the aqueous solution, on mixing with phenylhydrazine hydrochloride, gave a yellow flocculent substance, m.p. 151°. According to the literature, the reaction product of benzoylformic acid and phenylhydrazine melts at 153° [10].

Therefore, the isolation of benzophenone, benzoic acid, and benzoylformic acid shows that the liquid is a mixture of benzophenone and benzalacetophenone, the products of the ketonic cleavage of the unstable γ-ketol-1,1,2,4-tetraphenylbutyne-2-ol-1-one-4.

Distillation of the mixture of benzophenone and benzalacetophenone did not separate them because of the closeness of their boiling points (b.p. of benzophenone 305° [11], b.p. of benzalacetophenone 348° [12]. The semicarbazones of these substances also have similar melting points (benzophenone semicarbazone, m.p. 164° [12] benzalacetophenone semicarbazone, m.p. 168° [13]. The semicarbazone of the substance melts at 156-159° and is apparently a mixture of the two semicarbazones. It was found impossible to separate this mixture into the two individual components because of their similar solubility in the common solvents.

In order to answer the question when does the cleavage of the ethylenic γ-ketol take place, during its distillation or at the moment of its formation, the liquid product isolated from the acid solution of the transformation products of the pinacol was analyzed immediately after the distillation of the ether without vacuum distilling it.

Its molecular weight was found to be between 215-218. The molecular weight of benzophenone is 182, that of benzalacetophenone is 208, and that of the unsaturated γ-ketol, 390.

The same products, benzophenone, benzoic acid, benzoylformic acid were isolated from the reaction with aqueous potassium permanganate as from the previous oxidation. Pure semicarbazones and pyrazolines could not be obtained in this case because mixtures were formed.

SUMMARY

1. A new acetylenic pinacol (triphenylphenylacetylenylethylene glycol) was synthesized and its transformation in 30 and 35 % sulfuric acid studied.

2. It was shown that the pinacol rearranged in two ways: an acetylenic ketone, diphenylphenylacetylenylbenzoylmethane (1,1,2,4-tetraphenylbutyne-3-one-1) was formed by a pinacoline rearrangement, and an unstable ethylenic γ-ketol as a result of an acetylene-allene rearrangement.

3. It was proven that a phenyl group on the first hydroxylated carbon atom favors the pinacoline rearrangement (the formation of the acetylenic ketone), and the presence of a phenyl group on the second carbon atom, the acetylene-allene rearrangement (the formation of the ethylenic γ-ketol).

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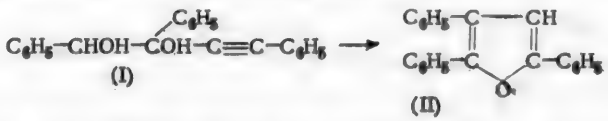
TRANSFORMATIONS OF SECONDARY-TERTIARY ACETYLENIC α-GLYCOLS PRODUCED BY MERCURY SALTS

II. 3-METHYL-5-PHENYL-PENTYN-4-DIOL-2,3

E. D. Venus-Danilova and V. M. Albitzkaya

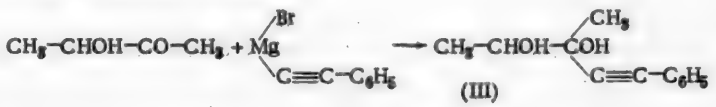
In a previous communication [1], it was shown that the acetylenic secondary-tertiary glycol, diphenylphenylacetylenylethylene glycol (I) (1,2,4-triphenyl-butyn-3-diol-1,2) was transformed into 2,3,5-triphenylpyran (II) by the action of an alcoholic solution of mercuric chloride.



(I) (II)

In order to see if this transformation was characteristic of other secondary-tertiary acetylenic glycols, the action of mercuric chloride upon 3-methyl-5-phenylpentyn-4-diol-2,3 (dimethyl-phenylacetylenylethylene glycol)(III) was studied under the analogous conditions.

Dimethylphenylacetylenylethylene glycol was obtained by the method of Iotsich from methylacetylcarbinol and phenylacetylenyl magnesium bromide.



(III)

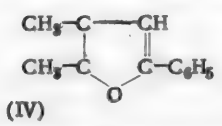
The glycol was obtained in two isomeric forms; one, m.p. 104-105°, was obtained as a first crop from a thick syrupy liquid, the other, m.p. 54-55°, separated after the mother liquor from the higher melting form was diluted with petroleum ether.

The higher melting (104-105°) modification of dimethylphenylacetylenylethylene glycol is reported in the literature [2], by F. Ya. Perveev, who synthesized it by hydrolyzing the corresponding α-oxide in very dilute hydrochloric acid.

Other cases where γ-glycols are formed in two or even three modifications, were reported by Du Pont [3] for tetramethylbutyndiol, and by A. I. Lebedeva and R. P. Riskina [4] for symmetrical dimethyl-di-p-tolylbutyndiol.

The two isomeric dimethylphenylacetylenylethylene glycols obtained are differentiated by different melting points, and by different rates of crystallization from dilute alcohol. Because of the presence of two assymmetric carbon atoms in the dimethylphenylacetylenylethylene glycol, four optical isomers and two racemic compounds are possible.

Only one product, 2,3-dimethyl-5-phenylfuran (IV) was obtained in identical yields (average 69 %) by the action of an alcoholic solution of mercuric chloride upon both forms of the glycol.



(IV)

The structure of the substance, b.p. of 108-112°, as a substitued furan, was proven by analysis and by the

formation of a maleic anhydride addition product, m.p. 194-195°.

The literature [5] gives an analogous boiling point for 2,3-dimethyl-5-phenylfuran and a m.p. of 195° for its maleic anhydride addition product.

It therefore follows, that dimethylphenylacetylenylethylene glycol (II) resembles diphenylphenylacetylenylethylene glycol (I) [1] in dehydrating and cyclyzing to a trisubstituted furan by the action of an alcoholic solution of mercuric chloride.

EXPERIMENTAL

1. The Synthesis of 3-Methyl-5-phenylpentyn-4-diol-2,5.

8 g of magnesium, 36 g of ethyl bromide, 34 g of phenylacetylene, and 14 g of freshly distilled methylacetylcarbinol were used in the synthesis.

The methylacetylcarbinol, in three volumes of dry ether, was added over a 2 hour period with strong mixing to the phenylacetylenyl magnesium bromide and the reaction mixture warmed slightly at the end of the reaction (25-35°). After 2 days, the resulting yellow brown thick mass was decomposed with ice and a solution of ammonium chloride, and extracted with ether. The ether extracts were dried with sodium sulfate. After removal of the ether, the phenylacetylene was distilled off at 12 mm, and 28-30°.

After 24 hours the thick syrupy mass partly crystallized. The crystals which separated were filtered on a glass filter, washed with a small quantity of petroleum ether, and recrystallized from 40% ethyl alcohol. The white crystalline substance, m.p. 104-105°, corresponds to the dimethylphenylacetylenylethylene glycol reported in the literature [2].

The syrupy mother liquor, after addition of the petroleum ether during the washing of the crystals, m.p. 104-105°, also crystallized on standing. The crystals were separated on a glass filter and recrystallized several times from40% aqueous ethyl alcohol until a constant melting point 54-55° was obtained.

Four runs were made under analogous conditions. The only modification was the cooling of the reaction mixture with water during the addition of the methylacetylcarbinol. The crystalline substance, m.p. 104-105°, separated after the removal of the ether and before the distillation of the phenylacetylene. The crystalline products obtained were much less discolored under these conditions.

The results of the synthesis are given in Table 1.

TABLE 1

Expt. No.	Quantities				Yield of the glycol				Total yield
	Magnesium (in g)	Ethyl bromide (in g)	Phenylacetylene (in g)	Methylacetylcarbinol (in g)	M.p. 105°		M.p. 55°		
					in g	in %	in g	in %	
1	8	36	34	14	8	26.7	3.5	11.7	38.4
2	8	36	34	14	3.5	11.6	10	33.3	44.9
3	6.8	31	29	12	–	–	15	57.7	57.7
4	6	27	25.5	10.6	–	–	12	52.7	52.7
	28.8	130	122.5	50.6	11.5	9.6	40.5	38.9	48.5

The total yield of 48.5% of the glycol is calculated on the basis of the methylacetylcarbinol used.

After several recrystallizations from petroleum ether and finally from aqueous alcohol, 9 g of the glycol, with m.p. 105°, and 27.5 g of the glycol with m.p. 55° were obtained.

Both of the products are readily soluble in ether, benzene, chloroform, and alcohol; they are poorly soluble in petroleum ether. In this solvent and in aqueous alcohol, the higher melting form is somewhat more insoluble than the lower melting form. Both forms decolorize a solution of bromine in chloroform and aqueous potassium permanganate.

Analysis of the substance with m.p. 105°. .
0.1471 g substance: 0.4047 g CO_2; 0.1030 g H_2O. Found %: C 75.05; H 7.80. $C_{12}H_{14}O_2$. Calculated %: C 75.79; H 7.36. 0.1894 g substance; 15.07 g C_6H_6: Δt 0.34°. Found: M 185. $C_{12}H_{14}O_2$. Calculated: M 190. 0.0164 g substance: 4.0 ml CH_4 (16°, 758.1 mm). Found: v_0 3.7 ml; % OH 17.30. $C_{12}H_{12}(OH)_2$. Calculated: v_0 3.8 ml; % OH 17.89.

2. Analysis of the substance with m.p. 55°.

0.1092 g substance: 0.3024 g CO_2; 0.0704 g H_2O. Found %: C 75.52; H 7.53. $C_{12}H_{14}O_2$. Calculated %: C 75.79; H 7.36. 0.1199 g substance; 13.68 g C_6H_6: Δt 0.23°. Found: M 187. $C_{12}H_{14}O_2$. Calculated: M 190. 0.0332 g substance: 8.5 ml CH_4 (20°, 759 mm). Found: v_0 7.7 ml; % OH 17.70. $C_{12}H_{12}(OH)_2$. Calculated: v_0 7.9 ml; % OH 17.89.

Fusion of the substance with m.p. 55° with potassium carbonate [6]. A mixture of 0.5 g of the substance and 0.28 g of potassium carbonate was heated on an oil bath in a flask containing an outlet tube. The substance began to decompose at a temperature of 190-195°. The decomposition products were introduced into an ammoniacal silver oxide solution, whereupon a copious white, flocculant precipitate of silver phenylacetylide formed.

On the basis of the analytical results, it can be seen that, when dimethylphenylacetylenylethylene glycol is synthesized by the method of Iotsich, a mixture of two isomers of this glycol are obtained in which the lower melting form predominates.

II. The Action of Mercuric Chloride on Dimethylphenylacetylenylethylene Glycol

Experiment 1. 0.4 g of mercuric chloride was added to a saturated alcoholic solution of 2 g, of the glycol with m.p. 105°, and the mixture heated on a boiling water bath for 8 hours in a closed tube. After this, the alcohol was distilled off. The residual greenish liquid was washed several times with water, extracted with petroleum ether, and dried with sodium sulfate. After removal of the ether, the reaction product was distilled at 4 mm, where it boiled at 108-112°.

Experiment 2. A saturated alcoholic solution of 2 g of the glycol, with m.p. 55° and 0.5 g of mercuric chloride were heated for 8 hours on a boiling water bath. The reaction products were isolated in the same manner as in Experiment 1. The product obtained also boiled at 108-112° at 4 mm.

The results of five experiments are given in Table 2. The duration of heating was 8 hours for all of the experiments.

TABLE 2

Expt. No.	Quantity			Yield of substance with b.p. 108-112° at 4 mm	
	$HgCl_2$ (in g)	Glycol with m.p. 105° (in g)	Glycol with m.p. 55° (in g)	(in g)	(in %)
1	0.3	1	–	0.6	66.7
2	0.5	–	2	1.2	66.7
3	0.5	–	2	1.2	66.7
4	0.4	2	–	1.3	72.2
5	0.8	–	4	2.5	69
	2.5	3	8	6.8	68

The substance, with b.p. 108-112° at 4 mm, when freshly distilled, is a clear, very slightly greenish liquid, which rapidly darkens on exposure to air. It decolorizes aqueous potassium permanganate and a solution of bromine in chloroform. It does not give a reaction for a carbonyl or a hydroxyl group. Strong sulfuric acid changes the substance into a brown, tarry liquid. A pine splinter moistened with hydrochloric acid is colored dark green by the vapors of the substance.

0.0921 g substance: 0.2814 g CO_2; 0.0617 g H_2O. Found %: C 83.37; H 7.38. $C_{12}H_{12}O$. Calculated %: C 83.72; H 6.99. 0.1613 g substance; 17.81 g C_6H_6: Δt 0.28°. Found: M 165. $C_{12}H_{12}O$. Calculated: M 172.

d_0^0 1.0094; d_{10}^{20} 1.0070; d_4^{20} 1.0092; n_D^{20} 1.58670. Found: MR_D 55.02. $C_{12}H_{12}O$. Calculated: MR_D 55.26.

The product of condensation with maleic anhydride was obtained by reacting 1.15 g of the substance, with b.p. 108-112° at 4 mm, with 0.86 g of maleic anhydride in anhydrous ether. After 16 days, the coarse, clear, prismatic crystals, m.p. 193-195°, described in the literature for the maleic anhydride addition product of 2,3-dimethyl-5-phenylfuran [5] were obtained.

On the basis of the analysis and the chemical properties of the product obtained, it can be considered that dimethylphenylacetylenylethylene glycol is transformed into 2,3-dimethyl-5-phenylfuran by the action of mercuric chloride in an average yield of 68%.

SUMMARY

1. When 3-methyl-5-phenylpentyn-4-diol-2,3 (dimethylphenylacetylenylethylene glycol) is synthesized by means of an organo-magnesium compound, two forms of the glycol are obtained: a higher melting form, m.p. 105°; and a lower melting form, m.p. 55°.

2. It was shown that both forms give 2,3-dimethyl-5-phenylfuran in identical yields by the action of mercuric chloride.

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COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

I. REACTION OF ETHYL β,β'-DIMETHYLGLYCIDATE WITH AMMONIA

S. N. Danilov and V. F. Martynov

The glycidic acids, as a new class of organic compounds, were discovered in 1880 by P. G. Melikov [1]. He obtained the simplest member of this class, glycidic acid, by the action of alcoholic potassium hydroxide upon a mixture of the two isomeric chlorolactic acids. A whole series of homologous glycidic acids was obtained by P. G. Melikov and other investigators, by the use of this method.

In 1904 Darzens [2,3], and a year later Claisen [4], worked out a more convenient method for preparing these compounds. They resulted from the action of α-halogen esters upon aldehydes and ketones in the presence of dry sodium ethylate (Darzens) and sodium amide (Claisen).

These methods of preparation made the glycidic acids readily available compounds.

The first steps in the study of the chemistry of this new class of compounds had already been taken in 1881 by P. G. Melikov [5,6,7]. He showed that, when ordinary glycidic acid was heated with aqueous ammonia to 120° in a sealed tube, the oxide ring was opened and aminohydroxypropionic acid formed. Similar reactions were made with a whole series of glycidic acids, but the structure of the reaction products was never ascertained. It was only much later that E. Fischer [8] determined the structure of the reaction product of ammonia and glycidic acid. The oxide ring is opened at the side furthest from the carboxyl group, with the product of the reaction being isoserine, $H_2NCH_2CHOHCOOH$. The structure was determined by reducing the reaction product with hydriodic acid, as a result of which β-aminopropionic acid was obtained.

Erlenmeyer [9] showed that β-phenylglycidic acid adds ammonia at room temperature to form β-phenylisoserine.

$$C_6H_5-CH-CH-COOH + NH_3 \longrightarrow C_6H_5-CH(NH_2)-CH(OH)-COOH.$$
(O)

The structure was determined by comparing the reaction product with one obtained by another synthesis. Phenylisoserine was prepared by the reduction of nitrosophenylpyruvic acid.

$$C_6H_5C(=NOH)COCOOH.$$

A similar reaction was repeated by Forster and Rao [10] in 1926 and again by Fourneau and Billeter [11] in 1940. In the latter instance ethyl β-phenylglycidate was used as the starting material. When it was reacted with aqueous ammonia at a temperature of 0-4°, the ester was changed to the amide in less than a half hour. If the reaction mixture was then allowed to stand at room temperature for several days, the oxide ring was opened with the formation of the amide of β-phenylisoserine.

From the above review of the reactions of the glycidic acids with ammonia, it is apparent that the oxide ring is extremely unstable. It is also evident that the reaction product from ammonia and glycidic acid could have been obtained without resorting to higher temperatures as Melikov did.

However, the reactivity of the oxide ring changes markedly if the β-carbon atom becomes tertiary. For example, it was shown by Claisen [12] that ethyl β,β'-phenylmethylglycidate did not have its oxide ring opened at room temperature by ammonia and only formed the amide with difficulty. Fourneau and Billeter, loc. cit., also pointed out the great stability of the oxide ring in similar glycidic acids. They also concluded that the now-accepted formulas for these compounds do not reflect their properties. Because of this some authors avoided working with glycidic acids containing a tertiary carbon atom in the β-position.

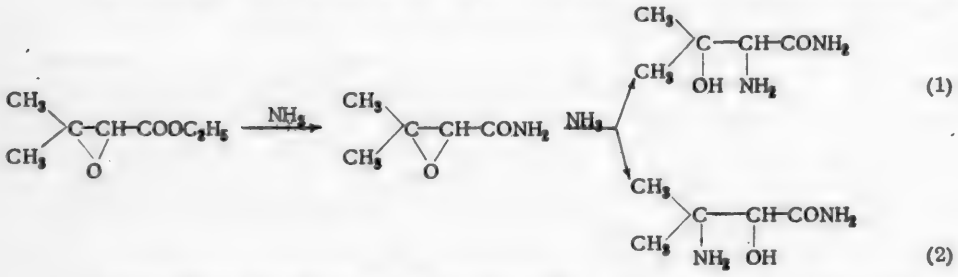
It was decided to fill this gap in the chemistry of glycidic acids by studying the action of ammonia upon glycidic acids with a tertiary carbon atom in the β-position. For the first example we took β,β'-dimethylglycidic acid ethyl ester. It is true, that Abderhalden [13] in 1934 studied the reaction of ammonia with β,β'-dimethyl-

glycidic acid, but when he obtained an uncrystallizable mixture, he did not investigate it any further.

First the reaction between ammonia and the ester of this acid at low temperatures was studied. The reaction was run in a closed tube with 30% aqueous ammonia for 4-5 hours at a temperature of 50°. In this way the amide of β,β'-dimethylglycidic acid was isolated in the form of white needlelike crystals. Finally the amide was obtained by shaking aqueous ammonia with the glycidic ester at room temperature for several hours. If the ammonia reacts with the glycidic ester at 100°, along with the formation of the amide, a splitting of the oxide ring occurs. After removal of the ammonia and the water, there results, not a crystalline substance as in the case of the amide, but a tar-like, uncrystallizable mass (as was reported by Abderhalden). In order to separate the product, the reaction mixture was dissolved in absolute ethanol and a stream of dry hydrogen chloride was passed into the solution. This resulted in separation of a crystalline precipitate which, as it was shown, turned out to be the hydrochloride of the amide of hydroxyaminoisovaleric acid (yield 51% of theory).

It is thus apparent that the oxide ring of this glycidic acid is opened at the relatively low temperature of 100°. Finally this reaction was effected in the absence of heat. The ammonia and the glycidic ester were allowed to stand at room temperature for a period of one month. The same product was obtained as when they were heated. Thus, the idea of the extreme stability of the oxide ring of glycidic acids containing a tertiary carbon atom in the β-position appears to be somewhat exaggerated.

In this case the opening of the oxide ring of the glycidic acid could occur in two separate directions.



The structure of the product had to be determined. This was done both directly and indirectly. The indirect method was to compare the product with one already reported in the literature. For this purpose α-amino-β-hydroxyisovaleric acid $(CH_3)_2C(OH)CH(NH_2)COOH$, which was prepared by Abderhalden [14] from β,β'-dimethylacrylic acid by means of a well-known literature method, was used. He also prepared the N-monobenzoyl derivative of this acid.

The free acid was prepared from the amide by hydrolysis with 50% sulfuric acid. The acid obtained melted at 259-260° in a closed capillary, while the acid obtained by Abderhalden melted at 218°. The monobenzoyl derivative of hydroxyaminoisovaleric acid was also obtained by reacting a solution of the amide in sodium hydroxide solution with benzoyl chloride, followed by the splitting of the amide linkage with nitrous acid. The benzoyl derivative obtained melted at 168-170°, while that of Abderhalden melted at 153°.

Therefore, it can be concluded that the product obtained is apparently the amide of α-hydroxy-β-aminoisovaleric acid.

Direct determination of the structure of the obtained product was made by reducing the hydroxyl to a hydrogen by means of hydriodic acid. Either α-amino- or β-aminoisovaleric acid should have been obtained. These are both well known and are readily distinguished by means of their melting points. α-Aminoisovaleric acid melts at 298°, the β-form at 217°. The product obtained melted sharply at 216-217°, and gave the correct analysis for aminoisovaleric acid.

Thus the second, direct, determination gives the same result as the first, indirect, method. This shows beyond doubt that the oxide ring of β,β'-dimethylglycidic acid is opened at the tertiary carbon atom by the action of ammonia, with the formation of the amide of α-hydroxy-β-aminoisovaleric acid.

EXPERIMENTAL

(With N. A. Rozepin and Z. M. Gofung)

Preparation of ethyl β,β'-dimethylglycidate. The method of Darzens, the reaction of acetone with ethyl

chloroacetate in the presence of alcohol free sodium ethylate was used. The yield in the best cases was 50%, based upon the ethyl chloroacetate which reacted.

After two redistillations the product boiled at 99-100° at 50 mm.

d_4^{20} 1.0110; n_D^{20} 1.4203; MR_D 36.70; calc. 36.75.

Reaction of β,β'-dimethylglycidate with ammonia in an aqueous medium. 10 g of ethyl β,β'-dimethylglycidate and 50 ml of 30% aqueous ammonia (d 0.885) were heated to 100° for 8 hours in a closed tube. The tube was then opened and its contents evaporated on a water bath in an evaporating dish. A clear brown tar resulted, which did not crystallize even on prolonged standing. The tarry product was dried in a vacuum desiccator and dissolved in absolute methanol. A stream of dry hydrogen chloride was passed into this solution over a 3 hour period. The reaction mixture warmed up and had to be cooled with ice water. The white precipitate of the hydrochloride of α-hydroxy-β-aminoisovaleric amide was filtered off and recrystallized from absolute alcohol. 5 g of well-formed, cubic crystals was obtained, which corresponds to 51% of theory.

0.4657 g substance: 54.4 ml 0.1 N H_2SO_4. 0.5163 g substance: 61.7 ml 0.1 N H_2SO_4. 0.1275 g substance: 0.1117 g AgCl. 0.1219 g substance: 0.1066 g AgCl. Found %: N 19.8, 20.3; Cl 21.17, 21.31. $C_5H_{13}O_2N_2Cl$. Calculated %: N 20.2; Cl 21.8.

Preparation of the benzoyl derivative. 0.5 g of the hydrochloride of α-hydroxy-β-aminoisovaleric amide was dissolved in a small amount of 10% NaOH. Benzoyl chloride, 1.2 g (1.5 times more than the theoretical) was added in small portions to the solution. The amount of benzoyl chloride was calculated for the dibenzoyl derivative. The reaction mixture was shaken violently. An insignificant amount of heat was given off. The unreacted benzoyl chloride was destroyed by warming the reaction mixture on the water bath. The reaction mixture was alkaline (tested with litmus).

The precipitate of the benzoyl derivative of α-hydroxy-β-aminoisovaleric amide (analysis showed that it was the monobenzoyl derivative) was filtered off on a Schott filter, carefully washed with water until completely alkaline-free, and recrystallized from absolute ethanol. 0.4 g of the monobenzoyl derivative of α-hydroxy-β-aminoisovaleric amide was obtained, which corresponds to 57 % of theory. M.p. 155-156°.

0.08 g substance: 8.45 ml N_2 (21°, 753 mm). 0.0836 g substance: 8.7 ml N_2 (23°, 772 mm). Found %: N 11.96, 11.97. $C_{12}H_{16}N_2O_3$. Calculated %: N 11.86.

Preparation of α-hydroxy-β-aminoisovaleric acid. 2 g of the hydrochloride of α-hydroxy-β-aminoisovaleric amide and 50 ml of 50% sulfuric acid (d 1.4) were heated for 7-8 hours in a round-bottomed flask with a reflux condenser. The SO_4^{2-} was removed with $BaCO_3$ until a negative reaction was obtained. The filtrate was evaporated on the water bath in an evaporating dish. A residue of a light-green, noncrystallizing, tarlike mass was obtained, which was dissolved in the minimum quantity of absolute ethanol after being dried in a vacuum desiccator. On cooling a white, halogen-containing (Beilstein test), finely-crystalline precipitate formed.

The halogen was removed with a silver sulfate solution. The AgCl precipitate was filtered off and the SO_4^{2-} was removed with $BaCO_3$ until a negative reaction for SO_4^{2-} was obtained. The filtrate was evaporated on the water bath in an evaporating dish. A tarry residue was obtained, which was dried in a vacuum desiccator and dissolved in absolute ethanol by prolonged heating. A finely crystalline, white precipitate separated on cooling. It was recrystallized from absolute ethanol. The product obtained did not contain halogen (Beilstein test).

0.3 g of α-hydroxy-β-aminoisovaleric acid was obtained, which corresponds to 20% of the theoretical yield. The melting point in a closed capillary was 259-260° (the substance darkens and gives off a considerable amount of gas).

0.0488 g substance: 4.6 ml N_2 (22°, 765 mm). 0.0670 g substance: 6.2 ml N_2 (22°, 762 mm). Found %: N 10.79, 10.56. $C_5H_{11}O_3N$. Calculated %: N 10.52.

Preparation of the monobenzoyl derivative of α-hydroxy-β-aminoisovaleric acid. An alcoholic solution of 0.5 g of the monobenzoyl derivative of α-hydroxy-β-aminoisovaleric amide was acidified with the minimum quantity of concentrated hydrochloric acid (acid to Congo) and treated with 0.2 g of $NaNO_2$ (the calculated quantity of $NaNO_2$ was used). The reaction mixture was shaken well and cooled with ice water. The reaction mixture

slowly became turbid, and then the crystalline precipitate of the monobenzoyl derivative of α-hydroxy-β-aminoisovaleric acid separated. The precipitate was recrystallized from a mixture of benzene and petroleum ether. It was extremely difficult to dissolve, and a prolonged period of heating on the steam bath was found necessary. 0.3 g of the substance was obtained, which corresponds to 60 % of the theoretical yield. M.p. 168-170°.

0.0566 g substance: 3.05 ml N_2 (22°, 762 mm). 0.1531 g substance: 8.3 ml N_2 (23°, 760 mm).
Found %: N 6.14, 6.13. $C_{12}H_{15}O_4N$. Calculated %: N 5.90.

Reduction of α-hydroxy-β-aminoisovaleric acid. 0.4 g of the substance, 8 ml of hydriodic acid (d 1.9) and 0.2 g of red phosphorus, were heated to 140-150° in a sealed tube for 5 hours. The tube was then opened (no inside pressure was observed). The colorless contents (the red phosphorus was all gone) of the tube were diluted with 100 ml of water and taken almost to dryness in vacuo. The residue was once more diluted with water and the halogen was removed with silver sulfate while the SO_4^{2-} was separated with $BaCO_3$ until a negative test was given. A pasty, tarlike mass remained in the dish. It was very soluble in water and insoluble in absolute alcohol and ether. It was dissolved by heating in aqueous ethanol and, after, standing for a week, a finely crystalline precipitate separated. It was recrystallized from aqueous ethanol. M.p. 205° in a closed capillary. After being dried for 3 hours at 110° its melting point was 216°. 0.7 g was obtained, which corresponds to 20% of theory. The preparation was repeated.

0.0587 g substance: 6.2 ml N_2 (20°, 748 mm). 0.0650 g substance: 6.7 ml N_2 (20°, 772 mm).
Found %: N 11.93, 12.01. $C_5H_{11}O_2N$. Calculated %: N 11.65.

SUMMARY

1. The reactions of ethyl β,β'-dimethylglycidate with aqueous ammonia have been studied. It was shown that when the glycidic ester was heated with 30% aqueous ammonia to 100°, the ester group was changed to the amide, and, at the same time, the oxide ring was opened. As a result, the amide of α-hydroxy-β-amino-isovaleric acid was formed.

2. The monobenzoyl derivative of the amide of α-hydroxy-β-aminoisovaleric acid, α-hydroxy-β-amino-isovaleric acid, and its monobenzoyl derivative were synthesized.

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STUDY OF COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

II. THE REACTION OF ETHYL β,β'-DIMETHYLGLYCIDATE WITH HYDROGEN SULFIDE

V. F. Martynov and N. A. Rozepina

Only a limited amount of studies have been devoted to the question of the reaction of hydrogen sulfide with compounds containing a three-membered oxide ring. The majority of these used ethylene oxide as the organic component. The papers of Chichibabin and Bestuzhev [1] and Nenitezescu and Scarlatescu [2] are included in this group, while Smith and Syöberg [3] used a more complex substance, glycide. As for the reaction of glycidic acids with hydrogen sulfide, there is nothing in the literature, even though these compounds may be of considerable interest.

A study of the reaction of hydrogen sulfide with glycidic acid containing a tertiary carbon atom in the β-position was undertaken. Ethyl β,β'-dimethylglycidate was chosen as the first representative, as it was the most readily available. Several methods were used to study the reaction of hydrogen sulfide with the above glycidic ester. A mixture of the glycidic ester and a saturated solution (in the cold) of hydrogen sulfide in aqueous ethanol was heated in a closed tube in the presence or the absence of mineral acids. In all of these cases no addition of hydrogen sulfide occurred, but the oxide ring hydrolyzed to form ethyl β,β'-dimethylglycerate. This reaction occurred even when the alcohol contained only traces of water. Only when absolute alcohol was used was the hydrolysis absent, but even then no addition of hydrogen sulfide occurred. The failure of these experiments is apparently due to the fact that glass tubes were used, and a large amount of hydrogen sulfide could not be placed in the reaction zone. The method of Smith and Syöberg [3] was then used. They found that the addition of hydrogen sulfide to the glycide occurred at room temperature in the presence of a large amount of $Ba(OH)_2$. Barium hydroxide acts as catalyst in this case, as there are many examples of the increase of the lability of the oxide ring under basic conditions.

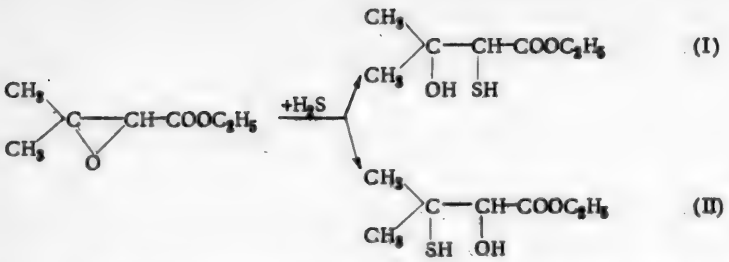
The following method was used: $Ba(OH)_2$, more than one mole per mole of glycidic ester, was mixed with a small amount of water and, while the solution was being stirred continuously, a stream of hydrogen sulfide was passed through it. After some time (2-3 hours) an alcoholic solution of the glycidic ester was added dropwise, while the stirring and the passage of hydrogen sulfide was continued. After completion of the addition of the glycidic ester, the hydrogen sulfide was passed in for 2-3 hours more. The barium was then completely precipitated with carbon dioxide, and the filtrate distilled until layers separated in the distillation flask. The lower layer appeared to be the reaction product and was extracted with ether.

A fractional distillation of the reaction products of several experiments revealed that the main part of the ethyl β,β'-dimethylglycidate had reacted with hydrogen sulfide. In each case only an insignificant quantity of the starting glycidic ester was recovered.

The sulfur-containing substance amounted to 70-75% of the theoretical. However, it was not a homogeneous substance, since on fractional distillation a series of fractions were obtained. The first of these, constituting almost half of the total amount, boiled over the narrow range of 97-99°, at 8 mm. The rest of the substance did not have a narrow-range boiling point, but distilled in the interval 130-175°.

The fraction with the boiling range of 97-99° had an unpleasant, penetrating odor. It gave a positive test for sulfur and for the mercaptan group (Reinboldt's test, mercuric mercaptide), and in all of the determinations (percent of total sulfur, mercury in the mercaptide, molecular weight, and molecular refractivity) it corresponded to ethyl hydroxymercaptoisovalerate.

In order finally to establish the structure of the compound, the position of the hydroxyl and mercapto group in the molecule had to be determined, as there are two possible ways in which the oxide ring could be opened:



The choice between the two formulas could have been made by determining the position of either the mercapto or of the hydroxyl group. It is well known from the literature that primary and secondary mercaptans give a red color with nitrous acid, while tertiary mercaptans give a green color. This is the qualitative test of Reinboldt [4]. No exception to this test has been found even though it has been tested with many types of compounds. The compound obtained gave a red coloration with this reaction and, on this basis, could be assigned the structure of Formula (I), ethyl α-mercapto-β-hydroxyisovalerate. In order to prove the correctness of Reinboldt's test, the position of the hydroxyl group in the molecule had to be determined.

To attain this, the mercaptan group had to be removed from the molecule, giving one of two possible acids; either β-hydroxyisovaleric or α-hydroxyisovaleric acid. Both of these acids are well known and can be distinguished from each other by the following property: β-hydroxyisovaleric acid is a syrup, while α-hydroxyisovaleric acid is a crystalline solid, melting at 86°. The mercaptan group was removed by the method of Mozingo [5] by heating the substance in alcohol with a large quantity of Raney nickel. As a result, an ethyl hydroxyisovalerate was obtained, which on saponification, gave an acid which did not crystallize even after a long period of standing (almost a month). Thus after the removal of the mercaptan group, β-hydroxyisovaleric acid was obtained.

The second method of determination agreed with the first. The oxide ring of ethyl β,β'-dimethylglycidate is opened by hydrogen sulfide in basic media at the site of the carboxyl group, and α-mercapto-β-hydroxyisovalerate is formed.

The nature of the higher boiling fraction could not be determined in spite of many attempts. It can be pointed but, however, that although these fractions contained sulfur, they did not give a test for the mercaptan group.

EXPERIMENTAL

Reaction of ethyl β,β'-dimethylglycidate with hydrogen sulfide in the presence of $Ba(OH)_2$. 20 g of $Ba(OH)_2$ was mixed with 100 ml of water, and a stream of hydrogen sulfide was passed into the mixture for 2 hours with continuous stirring. Then, while the stirring and the passage of hydrogen sulfide was continued, a solution of 40 g of the glycidic ester in 80 ml of ethanol was dropped in from a dropping funnel. The hydrogen sulfide was passed in for 3 hours more after all of the substance had been added.

The reaction mixture was allowed to stand overnight. The next day, a stream of carbon dioxide was passed in for 5 hours, with continuous stirring. The $BaCO_3$ was filtered off, the ethanol was distilled, and the reaction product separated at the bottom as an oily liquid. It was extracted with ether. The ethereal extract was dried with $MgSO_4$. After distillation of the ether, a vile-smelling liquid remained. This was vacuum distilled at 10 mm. Three fractions were obtained: 1) 97-99°, 10 g; 2) 140-150°, 7 g; 3) 165-170°, 3.7 g; 4) intermediate fractions, 1.5 g; and 5) residue in the distillation flask, 1.2 g. Total 23.4 g, corresponding to 47% of the theoretical. The first fraction analyzed as follows: d_4^{23} 1.097; n_D^{23} 1.46262; MR_D 44.56; calculated 44.03.

0.1173 g substance: 0.2325 $BaSO_4$. 0.2557 g substance: 0.3344 g $BaSO_4$. 0.1853 g substance: 17.61 g benzene: Δt 0.319°, 0.1411 g substance: 16.52 g benzene: Δt 0.255°. Found %: S 18.06, 17.96; M 171, 173.5. $C_7H_{14}O_3S$. Calculated %: S 18.02; M 178.

Mercuric mercaptide was obtained from the first fraction. The substance was shaken with three volumes of absolute ethanol and three times its weight of red mercuric oxide was added to it. The reaction proceeded

with the evolution of heat. A white precipitate of the mercaptide separated, which, after recrystallization from absolute ethanol, was analyzed for mercury.

0.1071 g substance: 3.9 ml NH_4CNS. 0.1118 g substance: 4.1 ml NH_4CNS. Found %: H 36.4, 36.65. $C_{14}H_{26}O_6S_2Hg$. Calculated %: Hg 36.21.

Removal of the sulfur from ethyl α-mercapto-β-hydroxyisovalerate. The sulfur was removed by the hydrolysis of the substance with Raney nickel according to Mozingo [5]. A catalyst of the highest activity was used.

6 g of the substance mixed with 60 ml of a suspension of Raney nickel in absolute ethanol (approximately 30-35 g of the catalyst). The mixture was refluxed for 8 hours, the catalyst was filtered off, and, after the removal of the alcohol, a fragrant liquid was obtained. It distilled over a one degree range at 62° and 7 mm. 3.5 g corresponding to 71.5% of theoretical was obtained. A negative test for a mercaptan group was obtained.

d_4^{20} 0.975; n_D^{20} 1.4187; MR_D 37.79, calculated 37.705.

The obtained ester was saponified by warming it with an alcoholic solution of sodium hydroxide. The resultant salt was acidified with dilute sulfuric acid and the free acid extracted with ether in an extractor. The ether extract was dried with magnesium sulfate and, after removal of the ether, a syrupy liquid with a sharp odor was obtained. It did not crystallize even upon standing for a month in a desiccator. The acid was analyzed as its silver salt:

0.1251 g substance: 0.0602 g Ag. 0.1543 g substance: 0.0744 g Ag. Found %: Ag 48.23, 48.35. $C_5H_9O_3Ag$. Calculated %: Ag 48.06.

SUMMARY

1. The reaction between hydrogen sulfide and ethyl β,β'-dimethylglycidate in the presence of $Ba(OH)_2$ at room temperature has been studied. It has been shown that under these conditions an addition of hydrogen sulfide occurs, with the formation of ethyl α-mercapto-β-hydroxy isovalerate.

2. It was shown that Reinboldt's test was valid for compounds containing a carboxyl and a carbomethoxyl group in the α-position to the mercaptan group.

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THE REACTION OF VINYLACETYLENIC α-OXIDES WITH OXYGEN-CONTAINING COMPOUNDS AND ORGANOMAGNESIUM COMPOUNDS

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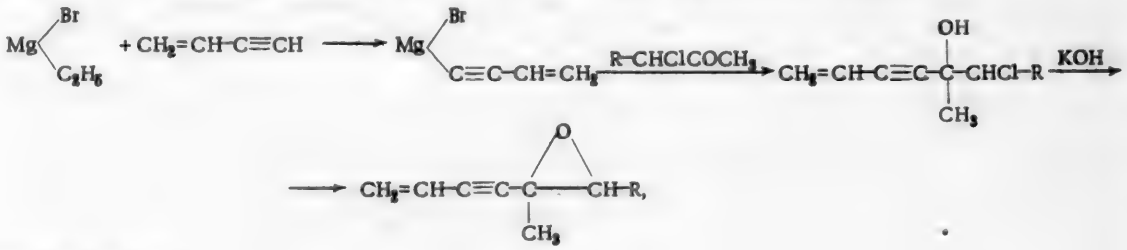
In spite of the large number of papers on the physical and chemical properties of oxides, no vinylacetylenic oxides have been reported up to the present time. It was considered expedient to find a method of synthesizing these compounds and to determine the influence of the vinylacetylene group on the reactivity of the oxide, and on the order of addition of various compounds. The synthesis of the oxides was accomplished by starting with vinyl acetylenic chlorohydrins, which were obtained by the reaction of the vinylacetylenyl magnesium halides with α-chloroketones and α-chloroaldehydes.

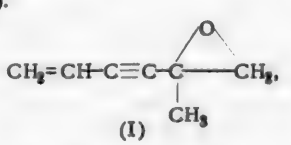
The condensation of vinylacetylene with chloroacetone and chloromethyl ethyl ketone (3-chlorobutanone-2) was studied. The synthesis of the oxide occurs according to the following equation:



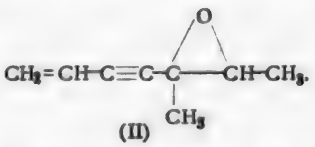
where R= H and CH_3.

The HCl was removed by the action of powdered potassium hydroxide on an ethereal solution. The oxides were obtained in yields of 80-85% based on the chloroketone used.

The oxides synthesized were 2-methylepoxy-1,2-hexen-5-yn-3 (I) and 3-methylepoxy-2,3-hepten-6-yn-4 (II).



(I)



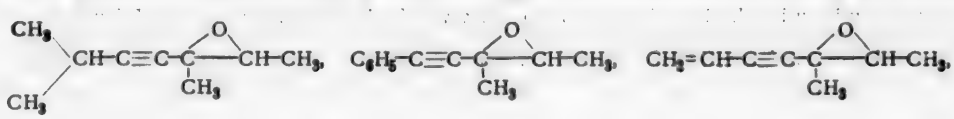
(II)

They are colorless liquids with a sharp odor. On exposure to the air they slowly thicken, and, after 2-3 months, form transparent, glasslike masses. They are thermally unstable, and, when heated above 140°, in the absence of a solvent, they explode.

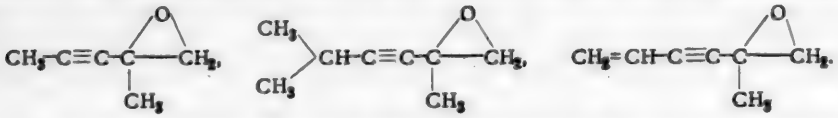
The oxides obtained are somewhat distinguishable by differences in reactivity. For example, 2-methylepoxy-1,2-hexen-5-yn-3 (I) decomposes explosively upon the addition of a crystal of ferric chloride, even at room temperatures. 3-Methylepoxy-2,3-hepten-6-yn-4 (II) remains unchanged in the presence of ferric chloride.

Oxide (I) is changed into the glycol by the action of water containing traces of hydrochloric acid, whereas oxide (II) is preferentially isomerized to the corresponding ketone under these conditions. The glycol is formed in the presence of traces of sulfuric acid. The addition of water to the oxides occurs readily. The reaction starts at room temperature and proceeds with the evolution of much heat.

The ease of the addition of water to ethylenic oxides, as was shown by Eltekov [2], depends on the number and the position of the substituents. It was shown [3] that the trisubstituted acetylenic and vinylacetylenic oxides



reacted much less readily with water in the presence of catalysts than did the disubstituted asymmetric oxides.



Several authors have proposed different mechanisms for the addition of water to the oxides. Zimakov [1] showed that ethylene glycol is formed by means of an intermediate compound (ethyl glycol sulfuric ester). However, this is a common characteristic. It is proposed that the catalytic activity of the various acids on the rupture of the oxide ring lies in the fact that the proton of the acid coordinates with the oxygen atom of the oxide ring, and the anion, by reaction with the water, generates hydroxyl groups which complete the splitting of the oxide ring by adding to the more polarized carbon atom. 2-Methyl-epoxy-1,2-hexen-5-yn-3 (I) easily adds aldehydes and ketones in the presence of ferric chloride, forming the corresponding acetals – dioxolanes.

The reaction of the oxides with acetone, methyl ethyl ketone, methyl isobutyl ketone, and mesityl oxide was studied.

The method used for the condensation of the ketones with the oxide is as follows: 1-2 g of the catalyst was added to three times the quantity of the ketone. The oxide was then added to it in small portions. The addition of the oxide was regulated so as to keep the reaction temperature below 40°. The mixture turned dark brown in color. The color was almost completely removed by washing the reaction mixture with an oxalic acid solution. The derivatives of methyl ethyl ketone and methyl isobutyl ketone had indeterminate boiling points.

3-Methylepoxy-2,3-hepten-6-yn-4 (II) did not react with ketones or aldehydes in the presence of ferric chloride. These reactions were found to occur comparatively easily when the catalyst was changed to sulfuric or oxalic acid. The following dioxalanes were obtained: derived from acetone, methyl ethyl ketone, and mesityl oxide. The above method was used for the synthesis of the dioxolanes, with the only change being the heating of the reaction mixture to 70° for 10-15 minutes after the addition of the oxide.

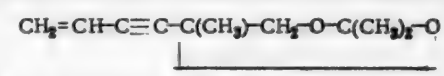
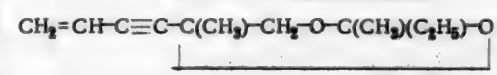
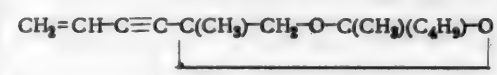
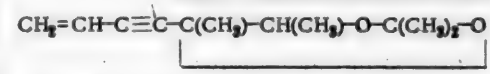
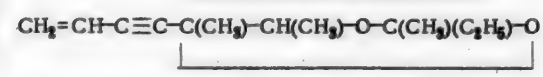
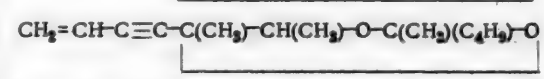
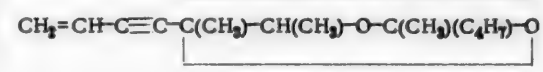
The dioxolanes were hydrolyzed to the corresponding glycol and ketone by warming them in 2% sulfuric acid. This served as a method for the determination of the structure of the products of the condensation between the oxides and the ketones. The ketones were identified by means of their 2,4-dinitrophenylhydrazones.

The cyclic acetals are colorless liquids with slight pleasant odors. They slowly turn yellow on exposure to air. They are thermally unstable, and explode when heated above 140°.

Acetoacetic ester does not react with the oxides in the presence of the above catalysts. The condensation reaction with chloroacetone proceeds smoothly without any tarring, but the reaction product is unstable and decomposes when it is heated in vacuum at 1-2 mm. The physical constants and the yields of the dioxolanes synthesized is given in the table. It is apparent that the yields of the condensation products of the oxides and ketones depend not only upon the structure of the oxide, but also upon the structure of the ketone. Asymmetric disubstituted vinylacetylenic oxides react more readily with ketones than do trisubstituted ones. The yield does not depend upon the chain length of the substituent, but upon its branching. For example, the derivatives of acetone and methyl ethyl ketone are obtained in yields of 52-57% whereas the yield of the derivative of methylisobutyl ketone never exceeds 25%. The isomerization products of the oxides, and small amounts of tars due to polymerization, were obtained as side reaction products in all of these condensations. The side products were not investigated further.

EXPERIMENTAL

2-Methyl-1-chlorohexen-5-yn-3-ol-2. 80 g of dry vinylacetylene was passed into a solution of ethyl magnesium bromide (1 mole) in ether with strong stirring and cooling with ice and water. The reaction mixture was allowed to stand overnight. 85 g of chloroacetone was then added slowly to it and the stirring continued for 3 hours more. The organomagnesium complex obtained was then carefully decomposed, with cooling, by 30% acetic acid. The ether layer was separated, washed with water, and dried with fused Na_2SO_4. After the removal of the ether, the residue was vacuum distilled. The chloroalcohol obtained had a b.p. of 70-71° at 5 mm. 76 g of the substance was obtained. The chloroalcohol was a colorless liquid which tarred badly on redistillation. Upon exposure it turned brown and slowly polymerized. It reacted explosively with silver nitrate in the presence of strong nitric acid.

No.	Formula	B.p.	d_4^{17}	n_D^{17}	MR_D	
					calculated	found
1		51-52°/5 mm	0.9448	1.4658	47.0	48.5
2		71-72°/4 mm	0.9440	1.4680	51.5	53.0
3		92-93°/5 mm	0.9378	1.4675	60.6	61.7
4		60-61°/5 mm	0.9225	1.4690	52.7	54.3
5		80-81°/5 mm	0.9390	1.4750	55.8	57.7
6		99-103°/10 mm	0.9391	1.4730	65.5	66.4
7		89-92°/3 mm	0.9515	1.4850	65.0	66.4

In view of this decomposition of the chloroalcohol upon redistillation, it was not isolated in the subsequent runs and the oxide was obtained directly from the dry ether solution of the chloroalcohol.

d_4^{20} 1.0816; d_4^0 1.1034; n_α^{20} 1.49976; MR_α 39.0; calculated 38.3.

0.1508, 0.1703 g substance: 0.1504, 0.1698 g AgCl; 0.0861 g substance: 14.22 ml CH_4 (11.9° 760 mm); 0.1339 g substance: 23.82 ml CH_4 (16.5°, 749 mm). Found %: Cl 24.7, 24.61; active H 0.703, 0.732. C_7H_9OCl. Calculated %: Cl 24.55; active H 0.700.

3-Methyl-2-chlorohepten-6-yn-4-ol-3 was obtained in a manner similar to the above. After two redistillations a product with a b.p. of 69° at 3.5 mm was obtained.

d_4^{20} 1.0606; d_4^0 1.1482; n_α^{20} 1.49416; MR_α 43.3; calculated 42.9

0.1839, 0.2405 g substance: 0.1631, 0.2147 g AgCl. Found %: Cl 21.9, 22.08. $C_8H_{11}OCl$. Calculated %: Cl 22.4.

2-Methylepoxy-1,2-hexen-5-yn-3 (I). 110 g of powdered potassium hydroxide was added in small portions with continuous shaking to a solution of 90 g of the chloroalcohol in 300 ml of absolute ether. The ether solution was then carefully poured off and the residue dissolved in water. The aqueous layer was twice extracted with ether. The ether extracts were added to the ether solution and dried over Na_2SO_4. The ether was distilled off. The residual oxide after two redistillations had a boiling point of 50-51° at 15 mm. Yield 72%.

d_4^{22} 0.9149; d_4^0 0.9377; n_α^{22} 1.47394; MR_α 33.17; calculated 31.3.

0.1048 g substance: 0.2910 g CO_2; 0.0870 g H_2O. Found %: C 77.48; H 9.51. C_7H_8O. Calculated %: C 77.75; H 9.39.

3-Methylepoxy-2,3-hepten-6-yn-4 (II). The oxide was obtained in the first run by using the above method. It boiled at 54-55° at 12 mm after two redistillations.

d_4^{20} 0.9005; n_D^{20} 1.4781; MR_D 38.41; calculated 36.82.

0.1034, 0.1537 g substance: 0.2973, 0.3084 g CO_2; 0.0778, 0.0875 g H_2O. Found %: C 78.14, 78.09; H 8.45, 8.45. $C_8H_{10}O$. Calculated %: C 78.63; H 8.25.

Later both of the oxides were obtained directly from the ether solution of the chloroalcohol without first isolating and redistilling it. $^3/_4$ of a mole of the chloroketone (chloroacetone or chloromethyl ethyl ketone) was added slowly, with strong stirring and cooling, to 1 mole of vinylacetylenyl magnesium bromide. After addition

of the chloroketone, the stirring was continued for 3-4 hours. The organomagnesium complex was decomposed with stirring and cooling by 30% acetic acid.

The ether layer was separated, and the water twice extracted with ether. The ether extracts were combined with the ether solution, washed with water, and dried. The ether solution was filtered and the oxide was obtained by the method given above. In this case the yield of the oxide was 85-87% of theory, based on the chloroketone used.

2-Methylhexen-5-yn-3-diol-1,2. 90 ml of water and 3 drops of hydrochloric acid were placed in a flask. 30 g of the oxide (I) was added in small portions with continuous shaking. An evolution of heat occurred. In order to avoid too much tarring, the flask was cooled from time to time in ice water. At the end of the reaction, the water was vacuum distilled, and the resultant dark-brown mass was placed into a crystallizing dish immersed in a freezing mixture (ice and salt). The crystals which separated were filtered off and recrystallized from benzene. After three recrystallizations, colorless crystals (17 g, 50% of the theoretical) with a m.p. of 48-49° and a b.p. of 81-82° at 3 mm were obtained.

0.1088 g substance: 40.62 ml CH_4 (12.5° 753 mm); 0.1097 g substance: 41.22 ml CH_4 (15.3° 766 mm); 0.1052, 0.1067 g substance: 0.2585, 0.2627 g CO_2; 0.0770, 0.0794 g H_2O. Found %: C 67.01, 67.15; H 8.19, 8.33; active H 1.573, 1.559. $C_7H_{10}O_2$. Calculated %: C 66.64; H 7.99; active H 1.587.

3-Methylhepten-6-yn-4-diol-2,3. The glycol was obtained under conditions similar to the above after working it up with water containing 5 drops of sulfuric acid. The reaction was accompanied by an evolution of heat but with less intensity then in the preceding case. The upper layer which formed, was removed and the aqueous layer was extracted with ether. The ether solution was added to the main fraction and dried with Na_2SO_4. The ether was removed and the substance obtained was vacuum distilled. After two redistillations, the glycol had a b.p. of 109-110° at 8 mm.

d_4^0 1.0166; d_4^{16} 1.008; n_D^{16} 1.5010; MR_D 41.2; calculated 39.6.

0.1066, 0.1012 g substance: 36.2, 34.2 ml CH_4 (14.5°, 756 mm). Found %: active H 1.423, 1.416. $C_8H_{12}O_2$. Calculated %: active H 1.438.

The glycol obtained was a viscous liquid which slowly crystallized. M.p. 20-21°. The crystals polymerized to a hard glasslike mass on exposure to the air.

Condensation of 2-methylepoxy-1,2-hexen-5-yn-3 (I) with acetone. 100 ml of acetone was placed with 1 g of ferric chloride in a round-bottomed flask with a reflux condenser and a mechanical stirrer. 20 g of the oxide was added slowly so as not to allow the temperature to rise above 40°. After all of the oxide was added, the stirring was continued for about one hour. The mixture was then washed with a solution of oxalic acid, and dried with Na_2SO_4. The acetone was removed in vacuum. After two redistillations, 16 g (52%) of the substance was obtained. Its constants are given in the table (Formula 1).

0.1063, 0.1105 g substance: 0.2806, 0.2922 g CO_2; 0.0822, 0.0846 g H_2O. Found %: C 71.99, 72.12; H 8.65, 8.57. $C_{10}H_{14}O_2$. Calculated %: C 72.26; H 8.49.

Hydrolysis of the dioxolane. 10 g of the dioxolane and 100 ml of a 2% solution of H_2SO_4 were placed in a round bottom flask with a mechanical stirrer and reflux condenser. The mixture was heated for 30 minutes. Acetone was separated from the products of the hydrolysis and identified by means of its 2,4-dinitrophenylhydrozone, which melted at 125°. A mixed melting point determination with an authentically prepared acetone 2,4-dinitrophenylhydrazone gave no depression.

Found %: N 23.7. $C_9H_{10}O_4N_4$. Calculated %: N 23.51.

The aqueous solution, after removal of the acetone, was distilled. The distillate was extracted with ether, the ether extracts were dried with Na_2SO_4, the ether was removed, and the residue vacuum distilled. Along with the glycol, a crystalline substance with a melting point of 91-92° and a b.p. of 81-82° at 3 mm was isolated. It gave a red coloration characteristic for enols with alcoholic ferric chloride, and could be titrated with dilute alkalis and sodium methylate.

Condensation of 2-methylepoxy-1,2-hexen-5-yn-3 (I) with methyl ethyl ketone. By the condensation of 30 g of the oxide with 50 ml of methyl ethyl ketone, 29 g (57%) of the dioxolane was obtained (Formula 2 in the table).

0.0997, 0.1102 g substance: 0.2674, 0.2952 g CO_2; 0.0781, 0.0857 g H_2O. Found %: C 73.15, 73.07; H 8.77, 8.70, $C_{11}H_{16}O_2$. Calculated %: C 73.30; H 8.95.

Methyl ethyl ketone was isolated from the hydrolysis products of the dioxolane and identified by means of its 2,4-dinitrophenylhydrazone with a m.p. of 110°, which gave no depression with an authentically prepared methyl ethyl ketone 2,4-dinitrophenylhydrazone.

Found %: N 22.40, 22.45. $C_{10}H_{12}O_4N_4$. Calculated %: N 22.20.

In addition, as in the first case, the dehydration product of the glycol was obtained.

Condensation of 2-methylepoxy-1,2-hexen-5-yn-3 (I) with methyl isobutyl ketone. The same method was used to condense 30 g of the oxide and 50 ml of methylisobutyl ketone. 14 g (25%) of the dioxolane (Formula 3 in the table) was obtained.

0.1034, 0.1058 g substance: 0.2820, 0.2887 g CO_2; 0.949, 0.965 g H_2O. Found %: C 74.39, 74.42; H 10.27, 10.21. $C_{13}H_{20}O_2$. Calculated %: C 74.60; H 10.11.

The hydrolysis products of the dioxolane were found to contain: 1) methyl isobutyl ketone, identified by means of its 2,4-dinitrophenyl hydrazone with a m.p. of 93-94°, which gave no depression in a mixed melting point determination.

Found %: N 19.99. $C_{12}H_{16}O_4N_4$. Calculated %: N 19.98

and 2) a crystalline product with a m.p. of 91-92°.

Condensation of 3-methylepoxy-2,3-hepten-6-yn-4 (II) with acetone. 100 ml of acetone and 4 g of oxalic acid were placed in a round bottomed flask with a mechanical stirrer and reflux condenser, and 20 g of the oxide was added slowly to it. The reaction temperature was kept around 40°. The mixture was then washed with aqueous sodium carbonate and dried with Na_2SO_4. The excess acetone was removed in vacuum and the residual dark brown product distilled at a temperature of 60-61° at 5 mm: 14 g (49%) of the substance was obtained. Its constants are given in the table (Formula 4).

0.1028, 0.1131 g substance: 0.2752, 0.3033 g CO_2; 0.0838, 0.0927 g H_2O. Found %: C 73.02, 73.13; H 9.12, 9.17. $C_{11}H_{16}O_2$. Calculated %: C 73.29; H 8.95.

The dioxolane was hydrolyzed with 2% H_2SO_4. The acetone 2,4-dinitrophenylhydrazone, m.p. 124°, which separated gave no depression in a mixed melting point determination. A ketone with a b.p. of 57-59° at 9 mm and an empirical formula of $C_8H_{10}O$, was isolated from the hydrolysis products.

d_4^{16} 0.9091; d_4^0 0.9207; n_D^{16} 1.4860; MR_D 38.5; calculated 36.7.

The semicarbazone of the ketone melted at 156-158° (with decomposition) after two recrystallizations from alcohol.

Found %: N 23.51, 23.47. $C_9H_{13}ON_3$. Calculated %: N 23.41.

In addition, a higher boiling fraction, b.p. 73-76° at 4 mm, which gave a red color characteristic for enols with an alcoholic solution of ferric chloride, was isolated from the hydrolysis products.

Condensation of 3-methylepoxy-2,3-hepten-6-yn-4 (II) with methyl ethyl ketone. The condensation was made using the above method. The reaction proceeded less energetically. After the addition of 25 g of the oxide, the reaction mixture was heated to 70° for 15 minutes. 13 g (33%) of the dioxolane, with a b.p. of 80-81° at 5 mm, was isolated (Formula 5 in the table).

0.978, 0.1018 g substance: 0.2651, 0.2763 g CO_2; 0.0798, 0.0845 g H_2O. Found %: C 73.93, 74.02; H 9.13, 9.23. $C_{12}H_{18}O_2$. Calculated %: C 74.19; H 9.34.

Methyl ethyl ketone was isolated from the hydrolysis of the dioxolane and characterized by means of its 2,4-dinitrophenylhydrazone, with a m.p. of 107-108°, which gave no depression in a mixed melting point determination.

Found %: N 22.45. $C_{10}H_{12}O_4N_4$. Calculated %: N 22.20.

The same products isolated from the acetone condensation were also obtained.

Condensation of 3-methylepoxy-2,3-hepten-6-yn-4 (II) with methylisobutyl ketone. The dioxolane was obtained by the condensation of 20 g of the oxide with a quantity (50 ml.) of methylisobutyl ketone under the same conditions. It had a b.p. of 99-103° at 10 mm. The yield was 3 g which corresponds to 8% of theory (formula 6 in the table).

0.1021, 0.1024 g substance: 0.2825, 0.2904 g CO_2; 0.0923, 0.0933 g H_2O. Found %: 75.46, 75.57; H 10.12, 10.20. $C_{14}H_{22}O_2$. Calculated %: C 75.63; H 9.95.

Methylisobutyl ketone was isolated on hydrolysis. Its 2,4-dinitrophenyl hydrazone melted at a temperature of 94-95°, and gave no depression in a mixed melting point determination.

Found %: N 20.01. $C_{12}H_{16}O_4N_4$. Calculated %: N 19.98

The dehydration products of the glycol were also isolated.

Condensation of 3-methylepoxy-2,3-hepten-6-yn-4 (II) with mesityl oxide. 8 g of the dioxolane (22%) with a m.p. of 89-92° was obtained from the condensation of 20 g of the oxide with mesityl oxide (Formula 7 in the table).

0.1043, 0.1054 g substance: 0.2911, 0.2939 g CO_2; 0.0874, 0.0869 g H_2O. Found %: C 76.12, 76.06; H 9.38, 9.21. $C_{14}H_{20}O_2$. Calculated %: C 76.32; H 9.15.

In addition, a fraction with a b.p. of 55-60° at 3 mm – a mixture of the ketone (isomerization product of the oxide) and the unreacted oxide – was obtained.

Upon hydrolysis of the dioxolane, the original mesityl oxide was isolated and characterized by means of its 2,4-dinitrophenylhydrazone with a m.p. of 199-200°, which gave no depression in a mixed melting point determination.

A considerable amount of a tarry product remained after the distillation of all of these dioxolanes. The distillation was made in the absence of air.

Condensation of methylepoxy-2,3-hepten-6-yn-4 (II) with methyl ethyl ketone in the presence of sulfuric acid. 50 ml of methyl ethyl ketone and 3-4 drops of sulfuric acid were placed in a round bottomed flask and 30 g of the oxide was slowly added to it. The reaction temperature rose to 60°. The mixture was then heated to 70° for 15 minutes, washed with aqueous sodium carbonate, and dried with Na_2SO_4. The excess of methyl ethyl ketone was removed in vacuum. The residue was distilled. 12 g of a substance with a b.p. of 58-62° at 4 mm, n_D^{18} 1.4940, (the product of the isomerization of the oxide – the ketone) and 23 g (49%) of the dioxolane with a b.p. of 78-80° at 4mm, n_D^{18} 1.4721, was obtained.

Methyl ethyl ketone and the product of the dehydration of the glycol were obtained from the products of the hydrolysis of the dioxolane. Thus, when 2-methylepoxy-2,3-hepten-6-yn-4 is reacted with methyl ethyl ketone in the presence of sulfuric acid, the yield of the dioxolane is greatly increased.

SUMMARY

1. Upon the reaction of vinylacetylenyl magnesium bromide with chloroacetone and chloromethyl ethyl ketone, the corresponding chloroalcohols, 2-methyl-1-chlorohexen-5-yn-3-ol-2 and 3-methyl-2-chloroheptene-6-yn-4-ol-3, were obtained.

2. The vinylacetylenyl oxides, 2-methylepoxy-1,2-hexen-5-yn-3 and 3-methylepoxy-2,3-hepten-6-yn-4, were obtained from these chloroalcohols by the action of powdered potassium hydroxide in ether solution.

3. The catalytic activity of ferric chloride, sulfuric acid, and oxalic acid upon the reaction of the oxides with ketones was studied. Some new dioxolanes, those of acetone, methyl ethyl ketone, methyl isobutyl ketone, and mesityl oxide, which are not reported in the literature, were obtained.

4. It was shown that the yields of the dioxalanes depends on the nature of the catalyst, the structural peculiarities of the oxides, and the structure of the ketone.

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NEW TYPES OF TERPENE TRANSFORMATIONS

IX. THE USE OF CHLOROTERPENES IN THE ORGANO-MAGNESIUM SYNTHESIS

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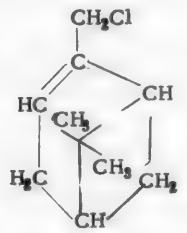
The chloroterpenes, initially obtained by the authors, are allylic chlorides suitable for a great variety of double decomposition reactions which may open up a new series of synthetic possibilities in the chemistry of terpenes. Some of these possibilities have already been realized [1]. The use of chloroterpenes in the organo-magnesium synthesis, in successful cases, would lead directly to a series of interesting syntheses of terpene derivatives of a definite structure, since rearrangements do not commonly occur during this reaction.

The task set is not a simple one. Allyl chloride, the prototype of the chloroterpenes, like other allyl halides, could not be reacted directly with magnesium for the preparation of homogeneous allyl magnesium chloride [2]. Later Yavorsky [3] avoided the difficulty of initially preparing the allyl magnesium halide and obtained allyl carbinols, although in low yields, by reacting a mixture of allyl bromide and a ketone with magnesium coated with ethyl bromide. He thus became the first to accomplish the synthesis originally proposed by Barbier [4]. Only in 1931 was Gilman [5] able to obtain an 80% yield of allyl magnesium chloride by using a large excess of magnesium, dilute ether solutions, and powerful stirring. Other researchers, repeating his work, could not obtain as high yields as he did [6].

Gilman was also the first to obtain allyl magnesium bromide in 89% yields, again by using very dilute ether solutions, a large excess of magnesium of a definite grade, and powerful stirring. Under other conditions, this yield could not even be approached [7]. Young, when studying the preparation of isobutenyl magnesium chloride, found that the yield dropped sharply when the reaction conditions were changed [8].

The above review shows that the use of allylic halides for reactions with magnesium is difficult, and this general problem has not been solved. The proper reaction conditions have to be found for each allylic halide. Any slight variation in these conditions will sharply affect the yield, or even make the reaction impossible. The magnesium has to be activated by coating with ethyl bromide, heating with iodine, etc. Allyl bromides will react more readily with magnesium than will allyl chlorides. For this reason the chloroterpenes will probably react less readily with magnesium than the corresponding bromoterpenes. Recognizing the great waste of time and reagents in survey experiments, the most readily available and stable of the chloroterpenes, myrtenyl chloride, was chosen for this study. Its preparation and properties were described earlier [9]. It is 10-chloro-α-pinene, $C_{10}H_{15}Cl$(A).



(A)

Throughout the rest of this paper the radical $C_{10}H_{15}$ represents the myrtenyl radical of the above structure.

In the reaction of magnesium with any halide, one or two reactions are possible:

(I) $R{-}Cl + Mg = R{-}Mg{-}Cl$; (II) $R{-}Mg{-}Cl + RCl = MgCl_2 + R{-}R$.

The yield from the first reaction may be determined by titrating an aliquot of the solution with acid; the yield of the second – by determination of the amount of inorganic chloride after the amount of the Grignard reagent has been found.

In order to find the conditions for myrtenyl chloride to react according to Reaction I, small amounts (2 g) of the chloride were used. Resublimed magnesium with a purity $>$ 99.8% was used in the form of shavings of 30-60 mesh.

The first series of experiments was run according to Yavorsky's conditions. A solution of myrtenyl chloride and acetone or benzophenone in ether was added to the magnesium covered by dry ether. The reaction temperature and the quantities of ether and magnesium were varied widely. Non-activated magnesium was used. In no case did either Reaction (I) or Reaction (II) occur.

The second series of experiments was also conducted according to Yavorsky's conditions, but the magnesium was initially activated with ethyl bromide. Sometimes the ethyl magnesium bromide was poured from the magnesium and replaced with dry ether, followed by addition of the ether solution of the myrtenyl chloride and the second component with stirring. At other times, the reaction was conducted without the removal of the ethyl magnesium bromide. In the experiments where the ethyl magnesium bromide was washed out, the yield of Reaction (I) (determined analytically by titration of the magnesium alcoholate with acid) approached zero with acetone and was about 30% with benzophenone.

Benzophenone and ethyl acetate were used as second components in the experiments where the ethyl magnesium bromide was not removed. In the case of benzophenone, the yield of Reaction (I) varied (the amount of ethyl magnesium bromide was taken into account) between 72-100%. Diphenylmyrtenylcarbinol was isolated as the reaction product (see Experimental; unsuccessful experiments are not reported). When the second component was ethyl acetate, the analytically determined yield was around 12%.

Apparently the yield of Reaction I under Yavorsky's conditions depends very much on the properties of the alcoholate of the tertiary alcohol that is formed. In the case of ethyl acetate, it rapidly precipitates from the solution as a sticky mass which covers the magnesium shavings and prevents any further reaction.

Repeated experiments in this direction showed that the chloride (A) reacts with magnesium activated by heating with 10% iodide to form up to 20% of $C_{10}H_{15}MgX$. When activated by coating with ethyl bromide (without removal of the C_2H_5MgBr), a yield up to 29% of $ClOH_{15}MgX$ was obtained. The yield in both cases was not constant, and depended upon the experimental conditions.

The activation causes the formation of some MgI_2 and $MgBr_2$ in the reaction medium, and cleans the surface of the magnesium. As was stated earlier, the chloroterpenes are allylic chlorides and easily take part in double decompositions. It was thought that when large amounts of $MgBr_2$ or MgI_2 were introduced into the reaction medium, the chloride (A) would be changed into the corresponding bromide or iodide, which would react more easily with the magnesium than the chloride. This hypothesis was verified. When the magnesium was initially treated with ether containing large amounts of bromine or iodine, it reacted with the chloride (A) almost completely. However, in the case of the bromine, the yield of Reaction (I) varied between 36-94%, depending on the amount of ether and on other factors. In the case of iodine, the yield did not exceed a certain percent because of the subsequent reaction according to Equation (II): $[C_{10}H_{15}MgI + C_{10}H_{15}I = (C_{10}H_{15})_2 + MgI_2]$.

In the interest of conciseness of this report, the results of the many separate experiments used to work out the final procedure are not given. Instead this procedure is given here: 30 g of dry bromine was slowly added, with cooling and mixing, to 50 g of magnesium turnings (not less than 99.8% pure; see below; 30-60 mesh) in 400 ml of dry ether (a round bottom flask with a reflux condenser, stirrer, and dropping funnel). After four hours of stirring at room temperature, a solution of 17 g of $C_{10}H_{15}Cl$ in 135 ml of dry ether was added. The stirring was continued for one hour more. An aliquot was removed and the yield of $C_{10}H_{15}MgX$ was determined by titration with 0.1 N acid in the presence of methyl orange (the yield usually was at least 70%). The $C_{10}H_{15}MgX$ solution was pumped over into another flask with dry nitrogen. The magnesium was washed twice with dry ether, covered with ether, and kept for the next experiment. The ether washes were added to the main solution. A triple adapter containing a stirrer, reflux condenser, and dropping funnel was attached and the second component was added.

When pure ($>$ 99.8%) magnesium was used, the yield of the $C_{15}H_{10}MgX$ did not vary over a wide temperature range (+5 – +25°). When technical magnesium was used, the yield fell and varied with the temperature of the reaction medium. For example, with one sample of commercial magnesium containing iron, not more than 45% of the possible yield, and then only at temperatures of +10 – +13° was obtained. Over +20°, the yield dropped because of Reaction II, and below +10° the reaction was slow and incomplete.

The myrtenyl magnesium halide was reacted with carbon dioxide, acetone, acetaldehyde, orthoformic ester, acetyl chloride, and formaldehyde. In the last three cases the expected product was not obtained (homomyrtenal, methylmertenyl ketone, or methyldimyrtenyl ketone, and homomyrtenol). Instead complex mixtures, which did not give constant boiling fractions on rectification, were obtained. The first four cases gave the following (respectively): 1) dimyrtenyl ketone; 2) dimethylmyrtenylcarbinol; 3) methylmyrtenylcarbinol; 4) phenylmyrtenylcarbinol. Unsuccessful experiments are not reported in the experimental section. Diphenylmyrtenylcarbinol was obtained by Yavorsky's method. The unusual nature of the chemical properties of myrtenyl chloride and myrtenyl magnesium halides is fully illustrated by the above. Almost none of its possible reaction products can be obtained by the usual methods, and very often it is necessary to devise special methods in order to realize the desired reaction.

EXPERIMENTAL

Synthesis of diphenylmyrtenylcarbinol by Yavorsky's method. 1 g of ethyl bromide followed by a solution of 4.3 g of benzophenone, and the chloride (A) in 18 ml of ether were added to 5.6 g of magnesium covered with dry ether. It was then stirred for 14 hours without heating. Two runs were made. The yield of $C_{10}H_{15}MgHal$ was 72% of theory in both cases (allowing for C_2H_5MgBr). The reaction products in both cases were decomposed with 1% hydrochloric acid, the ether layer separated, and the ether distilled. The residue solidified. It may have contained traces of benzophenone (m.p. 48°) and diphenylethylcarbinol (m.p. 94-95°). The crystals were recrystallized from hot alcohol and then twice from ether; m.p. 172-178°.

Found %: C 85.3; H 6.5. $C_{22}H_{20}O$. Calculated %: C 86.7; H 8.2.

The substance was considered to be impure diphenylmyrtenylcarbinol. The wide melting point range also showed that this was an impure substance.

Myrtenyl magnesium chloride and carbon dioxide. Commercial dry ice was added to a solution of myrtenyl magnesium chloride in ether prepared from 17 g of the chloride (A) by the previously given method (74% yield). The reaction product was allowed to stand overnight and then worked up in the usual manner. α-Pinene was obtained as the main product. This indicated that the commercial dry ice contained water and that carbon dioxide reacted less readily with myrtenyl magnesium chloride than water.

In the next run (chloride (A) 18 g; yield of $C_{10}H_{15}MgHal$ 69%) a stream of dry carbon dioxide was passed into the ether solution of the Grignard reagent until the formation of the precipitate ceased. The reaction product was decomposed with hydrochloric acid, the ether layer separated, and distilled at 0.1 mm. Besides lower boiling fractions none of which titrated bases, a fraction of b.p. 120-125°, a sticky liquid, was obtained.

d_4^{20} 0.972; n_D^{20} 1.5143.

Found %: C 84.5, 84.7; H 10.2, 10.6. $C_{21}H_{30}O$ (Dimyrtenyl ketone). Calculated %: C 84.5; H 10.1.

In an alalogous run, 5.9 g of this fraction was obtained.

Myrtenyl magnesium halide and acetone. An ether solution of 11 g of acetone was added to an ether solution of $C_{10}H_{15}MgX$ obtained from 17 g of the chloride (A), and the flask was heated to reflux for one hour. The ether and the magnesium alcoholate were poured from the magnesium and shaken with water. The ether layer was separated, dried with powdered potassium hydroxide, poured from the hydroxide, and finally distilled at 0.1 mm through a small column. One fraction with a narrow boiling range throughout was obtained. This fraction had a b.p. of 69-71°.

d_4^{20} 0.977; n_D^{20} 1.50226; MR_D 58.7. $C_{12}H_{21}OH$. F □ Calculated 59.3.

Found %: C 80.4, 80.0, 80.0; H 11.4, 11.4, 11.7; OH 8.5, 8.3 (Tserevitinov). $C_{12}H_{21}OH$. Calculated %: C 80.3; H 11.4; OH 8.8.

Myrtenyl magnesium halide and acetaldehyde. Technical magnesium containing iron was used in this synthesis because of a temporary lack of pure magnesium. After a long search, the proper conditions for the preparation of $C_{10}H_{15}MgHal$ in a 30-40% yield were found. They are given below.

56 g of magnesium, 400 ml of ether, and 20 g of bromine were mixed together with ice cooling. 20 g of the chloride (A) in 150 ml of ether was then added over a 45 minute period. The temperature inside the flask was kept at 10-13° (cooled with ice water when necessary), while the mixture was stirred for 45 minutes. Then 5.2 g of acetaldehyde in 30 ml of ether was added over a 40 minute period. After being allowed to stand over-

night, it was worked up in the usual manner. 13.8 g of reaction product was obtained. It was distilled at 5 mm through a small column. Two constant boiling fractions were obtained: Fraction I, b.p. 83-85°, 2.6 g.

d_4^{20} 0.9775; n_D^{20} 1.4998; MR_D 54.14. $C_{12}H_{19}OH\square$ Calculated %: C 54.67.

Found %: C 77.2, 76.9; H 10.7, 10.5. $C_{12}H_{20}O$. Calculated %: C 80.0; H 11.1.

Fraction II, b.p. 135-140°, 5.5 g.

d_4^{20} 0.953; n_D^{20} 1.5142; MR_D 85.37. $C_{20}H_{30}\square_2$. Calculated 85.6.

Found %: C 87.4, 87.5; H 11.3, 11.1. $C_{20}H_{30}$. Calculated %: C 88.8; H 11.1;

This substance was dimyrtenyl.

Myrtenyl magnesium halide and benzaldehyde. Resublimed magnesium and 18 g of chloride (A) gave 81% of $C_{10}H_{15}MgHal$. An ether solution of 10 g of benzaldehyde was added to the above ether solution, separated from the magnesium, and the contents of the flask refluxed for one hour. Dilute acetic acid was then added until the precipitate dissolved, the ether layer was separated, washed with aqueous alkali, dried with powdered potassium hydroxide, poured from the hydroxide, and finally distilled through a small column at 2 mm. 6.3 g of a fraction with b.p. 140-146° was obtained. On redistillation (at 0.1 mm), it came over at 120-121° (5.6 g).

d_4^{20} 1.003; n_D^{20} 1.5321; MR_D 74.83. $C_{17}H_{21}OH\square_4$. Calculated: 74.16.

Found %: C 85.6, 85.2; H 9.4, 9.6. $C_{17}H_{22}O$. Calculated %: C 84.2; H 9.2.

SUMMARY

1. Myrtenyl chloride was used as a model to study the possibility for using the allylic chloroterpenes, initially obtained by the authors, in organo-magnesium syntheses.

2. It was shown that Yavorsky's method was feasible in isolated cases but could not be generally used.

3. Conditions were found for the preparation of individual myrtenyl magnesium halides in yields not less than 70%.

4. Myrtenyl magnesium halide was reacted with carbon dioxide, acetaldehyde, and benzaldehyde, with the expected products being obtained.

With ethyl acetate, ethyl orthoformate, acetyl chloride, and formaldehyde, the proper reaction conditions for the preparation of the normal products could not be found.

The results illustrate, once more, the qualitative unusualness of the behavior of the chloroterpenes.

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NEW TYPES OF TERPENE TRANSFORMATIONS

X. SYNTHESIS OF HOMOTERPENES

D. Tishchenko and V. Foliadov

Homoterpenes result from the replacement of one or more hydrogen atoms of the terpenes by alkyl groups. Up to now they have been obtained by the reaction of organo-magnesium compounds with dihydroterpenyl aldehydes and ketones, followed by the removal of water from the secondary and tertiary dihydroterpenols that were formed. This method was used in a series of reactions by S. S. Nametkin and his students. However, it is not generally applicable, as the initial aldehydes and ketones are not always available, and may even be unknown. In addition, removal of water from the terpenol often leads to profound isomeric changes, so that the structure of the homoterpene obtained cannot be assigned only on the basis of the method of preparation.

Therefore, a method for the synthesis of the homoterpenes partly or entirely free from the above mentioned shortcomings was clearly desirable. Allylic chloroterpenes, obtained by the authors, contained replaceable chlorine atoms; for this reason, it was thought that they would easily react with organo-magnesium compounds to form homoterpenes:

$$C_{10}H_{15}Cl + ClMgR = C_{10}H_{15}R + MgCl_2.$$

It was shown previously (Communication IX) that the reaction between magnesium activated with iodine or bromine and the chloroterpenes was difficult to hold at the first level. Without the proper precautions, diterpenes are usually obtained in large amounts. Because of this, it could be considered that the authors' proposed synthesis of the homoterpenes was practical.

The equation cited above is only for the main reaction. It is well known that organo-magnesium compounds may act as reducing agents in a series of reactions, decomposing to an ethylenic hydrocarbon and HMgX. It is also quite clear that this reaction is between radicals, and that the free radicals R and R' can react among themselves to form R–R, R–R', and R'–R'. All of these reactions will lower the yield of the homoterpenes, and can be represented by the following equations:

$$CH_3CH_2MgX \longrightarrow CH_2{=}CH_2 + HMgX;$$
$$C_{10}H_{15}Cl + HMgX \longrightarrow MgXCl + C_{10}H_{16}\ (\text{terpene});$$
$$2C_{10}H_{15}Cl + 2CH_3CH_2MgX \longrightarrow 2MgClX + 2C_{10}H_{15}^{-} + 2C_2H_5^{-};$$
$$C_{10}H_{15}^{-} + C_2H_5^{-} \longrightarrow C_{10}H_{15}C_2H_5\ (\text{homoterpene});$$
$$2C_{10}H_{15}^{-} \longrightarrow C_{20}H_{30}\ (\text{diterpenyl});$$
$$2C_2H_5^{-} \longrightarrow C_4H_{10}\ (\text{butane}).$$

According to the particular organo-magnesium compound used, terpene, diterpenyl, the new homoterpene, the ethylenic hydrocarbon, or bisalkane are obtained. All of these side products will lower the yield of the homoterpene.

The experimental results agree with the above equations: upon the addition of the chloroterpene to the ether solution of the organo-magnesium compound, a continuous stream of gas, which contained the ethylenic and bisalkane hydrocarbons, separated. In two cases, the ethylenic hydrocarbon was absorbed in bromine and the corresponding dibromoalkanes isolated. In all cases, lower boiling fractions containing the terpene corresponding to the chloroterpene were obtained. The diterpenyl was obtained in all cases. Nevertheless the yield of the desired product was fully acceptable in all cases and varied between 40 and 60%.

In order to ascertain the conditions for the synthesis of the homoterpenes, the reaction of 6-chlorodipentene with methyl, ethyl, n-propyl, and n-butylmagnesium halides was used and a series of 6-alkylditerpenes prepared. They are all liquids with reasonably pleasant odors. Their physical properties are listed in the table.

The structure of the homoterpenes as 6-alkyldipentenes was based on the conditions of the reaction. It is well known that organo-magnesium syntheses generally occur without isomerization.

Only the synthesis of n-propyldipentene is given in the experimental section, in order to conserve space. The other syntheses were effected in an analogous fashion.

EXPERIMENTAL

n-Propyl magnesium bromide was prepared from 5.0 g of magnesium and 29 g of propyl bromide in 50 ml of ether, in a round-bottomed flask with a reflux condenser, stirrer and dropping funnel. 20 g of 6-chlorodipentene in 30 ml of ether was then added to it with stirring. The gas which separated was collected (1370 ml). The flask was then heated to reflux for two hours, whereupon a crystalline precipitate of magnesium halide dietherate came out. 1200 ml of the gas was passed into bromine; 550 ml, i.e. 54%, was absorbed. The bromine was washed out of the dibromide with sodium sulfite and 4 g of a dense liquid boiling entirely at 140°, which corresponds to 1,2-dibromopropane, was obtained. The contents of the flask were ice-cooled, decomposed with water, and acidified to litmus with dilute nitric acid. 4.0 g of chloride ion was found in the water layer; a 96% reaction occurred. The ether was removed from the ether layer; weight of the residue, 20 g; it was distilled through a small column (4-5 theoretical plates) at 3 mm: the 1st fraction 58-68.5°, 0.75 g, d_4^{20} 0.855 contained chlorine; the 2nd fraction 68.5-82°, 0.70 g, d_4^{20} 0.850, contained chlorine; the 3rd fraction 82-85°, 9.1 g, d_4^{20} 0.858, n_D^{20} 1.4765, MR_D 58.65, $C_{13}H_{22}Cl_2$, calculated: 59.10, contained chlorine. The rest of the fractionation was done in a flask with a side tube at a pressure of about 0.001 mm: the 4th fraction, up to 60°, d_4^{20} 0.8524; the 5th fraction 60-118°, 0.4 g; the 6th fraction 118-125°, 3.9 g, d_4^{20} 0.920, n_D^{20} 1.5134.

1. Physical properties of the 6-alkyldipentenes

Alkyldipentene	Boiling point (in °C)	Pressure (mm)	d_4^{20}	n_D^{20}	ΣMR_D
$C_{10}H_{16}$	70-71	20	0.8436	1.4734	–
$C_{10}H_{15}CH_3$	74-76	14	0.8466	1.4748	+0.05
$C_{10}H_{15}C_2H_5$	46-47	0.75	0.8489	1.4760	+0.05
$C_{10}H_{15}C_3H_7$	56-57	0.4	0.8469	1.4755	+0.18
$C_{10}H_{15}C_4H_9$	79-80	1.3	0.8488	1.4757	+0.10

Found %: C 88.2; H 11.9; M 253, 252. $C_{20}H_{30}$. Calculated %: C 88.8; H 11.2; M 260.

Fractions 1 and 2 were combined, the mixture containing 0.35 g of chlorodipentene. The mixture was distilled at 762 mm. The main fraction boiled at 178-182°: d_4^{20} 0.851; n_D^{20} 1.4780; MR_D 45.28. $C_{10}H_{16}$. Calculated 45.24.

Fractions 3 and 4 were combined and allowed to stand with metallic sodium ribbon for three weeks, and then distilled at a pressure of about 0.4 mm. 7.0 g was distilled, yielding: 1st fraction, to 56.5°, 0.5 g; 2nd fraction, 56.5-57.5°, 5.85 g.

For the fraction with b.p. 56.5-57.5°, 5.85 g,

d_4^{20} 0.8469; n_D^{20} 1.4755; MR_D 59.284.
$C_{13}H_{22}Cl_2$. Calculated: 59.098. EMR_D + 0.186.
Found %: C 87.5, 87.3; H 12.6, 12.6. $C_{13}H_{22}$. Calculated %: C 87.55; H 12.45.

The yield of the second fraction (propyldipentene) was about 30%, for the other alkyldipentenes from 40 to 60%.

SUMMARY

1. A new method for the synthesis of homomoterpenes by the reaction of allylic chloroterpenes with organo-magnesium compounds is given. The yield of the alkylpentenes was from 30-60% of the possible. The side products obtained were an alkane, an alkene, a terpene, and a diterpenyl.

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BROMINATION WITH DIOXANE DIBROMIDE

I. THE BROMINATION OF PHENOLS

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The monobromination of phenols by the usual methods is a difficult task. It is almost impossible to obtain monobromophenols by direct bromination in acidic and neutral media; on shifting to basic media, the problem is further complicated by the concurrent oxidative processes. On brominating phenols in organic solvents such as glacial acetic acid, chloroform, carbon disulfide, etc., monobromo derivatives are obtained in certain cases (p- and o-bromophenol and bromohydroquinone). However, many especially polyhydric phenols (resorcinol, pyrocatechol, pyrogallol, and phloroglucinol) form the polybromo compounds at once. For these reasons the determination of a general method for the monobromination of phenol appeared to be an interesting problem. The literature contains several papers dealing with the monobromination of phenols. Thus in 1923 complex compounds of bromine and salts of pyridine, and quinoline (pyridine-dibromide hydrobromide, $C_5H_5NBr_2 \cdot HBr$) were used as brominating agents for the bromination of pyrocatechol, resorcinol, and pyrogallol [1]. The bromination with these reagents is effected in glacial acetic acid solutions at room temperature. Pyridine dibromide hydrobromide only monobrominates pyrocatechol; resorcinol and pyrogallol form dibromides. Monobromoresorcinol and monobromopyrogallol could only be obtained by using quinoline dibromide hydrobromide. It was recently shown that pyridine dibromide hydrobromide brominates 2-naphthol to 6-bromo-2-naphthol (yield 45.5%). It is interesting to point out that phenol, under the action of this reagent in [illegible] glacial acetic acid solution, forms tribromophenol instantly [2]. The main drawback in the method of bromination with the complex pyridine and quinoline bromides lies in the difficulty in isolating the monobromophenols from the reaction mixture, as many of them are extremely soluble in water and are very poorly extracted with the ether from the dilute aqueous acetic acid. These authors do not give any yields of the monobromophenols in most cases, and it is therefore difficult to judge the value of this method. N-Bromoacetamide [3] and N-bromosuccinimide [4] were used for the monobromination of phenols and certain phenolic ethers. Monobromo derivatives were obtained in all cases (phenol, anisole, phenetole, 3-methoxytoluene, 1,4-dimethoxybenzene, 1- and 2-methoxynaphthalene, and several others). However, the yields by this method were often very low: for example, for anisole, a 32% yield of p-bromoanisole; for phenetole, a 20% yield of p-bromophenetole; and for 3-methoxytoluene, a 49% yield of the 6-bromo derivative. Also, the reagents themselves cannot be considered common and readily available.

An interesting method of bromination by means of a mixture of dichlorourea and potassium bromide in a weakly acidic aqueous or nonaqueous medium, was proposed M. V. Likhosherstov [5]. However this method was not worked out in detail for phenols, the author only using it for the mono-, di-, and tribromination of phenol and resorcinol.

In the present paper are reported the results of using dioxane dibromide, recently proposed as a convenient means for the bromination of organic compounds [6], as a brominating agent for all phenols. Dioxane dibromide - a molecular compound of dioxane and bromine, composition $C_4H_8O_2 \cdot Br_2$ – was first reported by Favorsky [7]. Dioxane dibromide is very easily obtained by simply mixing equivalent amounts of dioxane and bromine in solvents (excess of dioxane, ether, dichloroethane, etc.) or without solvents. It is a light orange, crystalline substance, m.p. 66°. It has to be stored in glass stoppered jars or in sealed ampoules. Samples of dioxane dibromide can be stored for a long time without loss of activity. Dioxane dibromide is readily soluble in pyridine, dioxane, chloroform, dichloroethane, and carbon tetrachloride, and somewhat less soluble in ether.

When dioxane dibromide is first dissolved in ether, a transparent orange solution forms, but after some time the liquid becomes turbid and separates into two layers: a lower dark red, dense layer; and an upper transparent ether layer. The lower layer is insoluble in water, and rapidly forms a colorless solution containing bromide ions with alkali. The lower layer retains the brominating activity. The nature of this phenomenon

has not been studied further as yet. Dioxane dibromide is very poorly soluble in water. Water solutions of it gradually decompose in several days. The decomposition is more rapid when the water is boiled. It volatilizes in the air.

As a brominating agent, dioxane dibromide has many advantages in comparison to bromine and other brominating agents. It is extremely easy to prepare and very easy to weigh out; it is practically non-hazardous to work with, and is easily handled and stored.

The action of dioxane dibromide on monohydric phenols and their ethers was first studied. Phenol reacts extremely easily with dioxane dibromide. The reaction can be effected in ether and dioxane solutions, or without solvents. When one equivalent of phenol is used, monobromophenol is formed in all cases. It must be pointed out, however, that for the preparation of the para isomer, the reaction is best run in ether solution or without solvents, while cooling the reaction mixture with cold water. Significant amounts of the ortho isomer are formed without the cooling. When two or three equivalents are used for the bromination, the excess dioxane dibromide does not react, and the only reaction product is monobromophenol.

Anisole, analogously to phenol, is brominated very easily in the cold to p-bromoanisole. In this case, the bromination can also be effected either in ether or without solvents. With other phenols, thymol is brominated to 4-bromothymol, and 1,3,5-xylenol to 4-bromo-1,3,5-xylenol. The yields of the monobrominated products are from 75 to 95%.

The dihydric phenols, hydroquinone, resorcinol, and pyrocatechol are readily brominated by dioxane dibromide. The bromination is more expedient when run in ether solution. It must be pointed out that monobromopyrocatechol and monobromoresorcinol are extremely difficult to crystallize. Crystalline products are only formed after the oil obtained initially is allowed to stand for long periods of time in a vacuum desiccator over sulfuric acid. However, once crystallized, the products behave normally and can easily be recrystallized from petroleum ether. K. Rosenmund [1] and N. V. Likhosherstov [5] also mention the difficult crystallization of 4-bromoresorcinol and 4-bromopyrocatechol. Apparently the difference between these compounds and the closely related bromohydroquinone can be explained by the contamination of 4-bromoresorcinol and 4-bromopyrocatechol by slight traces of other possible isomers. Besides the above, other dihydric phenols, orcin and guaiacol were also brominated. Orcin forms 2-bromoorcin in a 90% yield. Guaiacol—5-bromoguaiacol.

The use of two or more equivalents of dioxane dibromide for the bromination of the dihydric phenols, as for example hydroquinone, leads to the formation of dibromohydroquinone; higher brominated products are not formed.

The monobromination of the trihydric phenols has been the least studied. Only the monobrominated derivative of pyrogallol is known. Only tribromo derivatives were obtained from phloroglucinol and hydroxyhydroquinone. The action of dioxane dibromide on the simplest of the trihydric phenols, pyrogallol, hydroxyhydroquinone, and phloroglucinol, was studied. The bromination of pyrogallol is the smoothest, giving excellent yields of 4-bromopyrogallol or 4,6-dibromopyrogallol depending on the quantity of dioxane dibromide used. A strong darkening occurs on the bromination of hydroxyhydroquinone even in dilute ether solutions at 0°. No definite products could be isolated from the dark brown reaction mixture. Apparently in this case, along with the bromination, a simultaneous oxidation of the hydroxyhydroquinone, which is particularly unstable to oxidation, occurs.

In contrast to hydroxyhydroquinone, phloroglucinol brominates very smoothly, the use of one or two equivalents of the reagent leading to the formation of only one product, which, according to its bromine content, is dibromophloroglucinol. This compound was previously unreported. Whether or not phloroglucinol reacts in this case as a phenol or in its tautomeric carbonyl form, is not clear; this question needs further study. Dibromophloroglucinol is very soluble in ether, alcohol, and other common organic solvents; it is poorly soluble in cold water, and is crystallized from boiling water in the form of fine needles, m.p. 146°.

The action of dioxane dibromide on certain naphthols and hydroxyphenanthrenes was also studied. 1-Naphthol, 2-naphthol, and nerolin brominate well with dioxane dibromide in dioxane solution to form the respective 4-bromo-1-naphthol, 1-bromo-2-naphthol, and 1-bromonerolin in high yield.

The bromination of the hydroxyanthraquinones was somewhat more difficult. 1-Hydroxyanthraquinone, 2-hydroxyhydroquinone, 1,2-dihydroxyanthraquinone (alizarin), and 1,5-dihydroxyanthraquinone (anthrarufin) were brominated. To produce the monobromo derivatives, it was necessary to heat an equivalent molecular

mixture of the components to 50-60° for a short time. Analogous to the hydroxyanthraquinones, the bromination of phenols with a negative substituent-nitrophenol, salicylic acid – was done by heating to 50-60°. These compounds form only monosubstituted products even with large excesses of the reagent.

EXPERIMENTAL

Preparation of dioxane dibromide. 500 g of redistilled dioxane was placed in a 2-liter porcelain beaker, and 990 g (317 ml) of bromine was rapidly added with stirring and cooling with ice water. The hot dark brown solution obtained was poured with stirring into 2 liters of ice and water. A crystalline orange precipitate formed. It was filtered, pressed carefully, first on the filter, and then to dryness on a porous plate. The yield of dioxane dibromide was 1400 g (94%) m.p. 60°.

Bromination of phenol. 25 g of dioxane dibromide was added in small portions with shaking and water cooling to 9.4 g of crystalline phenol. The mixture liquified and HBr was given off. After the addition of all of the reagent, the mixture was poured into water and extracted with ether. The ether extract was dried with calcium chloride, and, after removal of the ether, was vacuum distilled. 15 g (88%) of p-bromophenol was obtained; b.p. 115-117° at 11-12 mm; m.p. 64-65°.

Bromination of anisole. 10.8 g of anisole was brominated with 25 g of dioxane dibromide in a manner analogous to phenol. The reaction mixture was washed with dilute sodium hydroxide solution and water; the oil separated, dried with calcium chloride, and vacuum distilled. 10.7 g (57%) of p-bromoanisole was obtained, b.p. 99-100° at 18 mm; n_D^{20} 1.5631.

Bromination of thymol (1-hydroxy-3-methyl-6-isopropylbenzene). 8.3 g of dioxane dibromide was added with shaking to 5 g of thymol dissolved in 10 ml of dioxane. The mixture was poured into water and extracted with ether. The ether extract was dried with anhydrous magnesium sulfate and the ether evaporated. The residual oil crystallized after standing in a vacuum desiccator over sulfuric acid. 7 g (90%) of 4-bromothymol (4-bromo-1-hydroxy-3-methyl-6-isopropylbenzene) was obtained, m.p. 55-56° (from petroleum ether).

Bromination of 1,3,5-xylenol. 12.2 g of xylenol was dissolved in ether and brominated with 25 g of dioxane dibromide. After addition of all of the reagent, the mixture was washed with water and dried with anhydrous magnesium sulfate. After removal of the ether, it was vacuum distilled. 15 g (75%) of 4-bromo-1,3,5-xylenol was obtained, b.p. 116-118° at 18-20 mm; m.p. 54°.

Bromination of hydroquinone. a) An ether solution of 5 g of dioxane dibromide was dropped with shaking and cooling into 2.2 g of hydroquinone dissolved in ether. The transparent solution obtained was washed with water, dried with calcium chloride, and the ether evaporated, 3.4 g (90%) of bromohydroquinone was obtained; m.p. 109° (before recrystallization), m.p. 110-111° (from n-heptane). b) 2.2 g of hydroquinone in ether was brominated with 10 g of dioxane dibromide. 4.82 g (90%) of 2,6-dibromohydroquinone was obtained; m.p. 164° (before and after recrystallization from water).

Bromination of pyrocatechol. A solution of 25 g of dioxane dibromide in 50 ml of ether was added with shaking to 11 g of pyrocatechol dissolved in 50 ml of ether. The mixture was washed several times with water, dried with anhydrous magnesium sulfate, and freed from the ether. The thick lightly colored oil obtained crystallized after a prolonged stay in a vacuum desiccator over sulfuric acid. 17 g (85%) of 4-bromopyrocatechol was obtained; m.p. 82° (before recrystallization), 86-87° (from petroleum ether).

Bromination of resorcinol. a) 1.1 g of resorcinol in 15 ml of ether was brominated by 2.5 g of dioxane dibromide in 20 ml of ether. The lightly colored mixture obtained was washed with a sodium sulfite solution and water, dried with anhydrous magnesium sulfate, and the ether evaporated. The residual oil crystallized only after a prolonged stay in a vacuum desiccator over sulfuric acid. 3.7 g (97%) of 4-bromoresorcinol, m.p. 101-102°, was obtained. b) 1.1 g of resorcinol in 20 ml of water was brominated with 4.96 g of dibromo dioxane. 2.48 g (93%) of 4,6-dibromoresorcinol was obtained, m.p. 110-112° (from water).

Bromination of orcin (2,6-dihydroxytoluene). 3.2 g of orcin in ether solution was brominated with 5.2 g of dioxane dibromide. The mixture was washed with water, dried with anhydrous magnesium sulfate, and the ether evaporated. The residual oil rapidly crystallized in vacuum desiccator over sulfur acid. 4 g (90%) of 2-bromo-orcin (2-bromo-3,5-dihydroxytoluene) was obtained; m.p. 134-135°.

Bromination of guaiacol (1-methoxy-2-hydroxybenzene). 12.6 g of guaiacol in ether was brominated with 25 g of dioxane dibromide. After washing, drying, and ether distilling, the residue was vacuum distilled. 18 g

(88%) of 5-bromoguaiacol (5-bromo-2-methoxy-2-hydroxy-benzene) was obtained: b.p. 170-174° at 15-18 mm; m.p. 44-45° (from petroleum ether).

Bromination of pyrogallol. a) 1.26 g of pyrogallol was brominated in ether with 2.5 g of dioxane dibromide. After processing in the usual manner and evaporating the ether, 1.95 g (95%) of 4-bromopyrogallol was obtained; m.p. 140° (decomp.). b) 1.26 g of pyrogallol in ether solution was brominated with 5 g of dioxane dibromide. 2.64 g of dibromopyrogallol was obtained, m.p. 149-150° (from benzene).

Bromination of phloroglucinol. 1.26 g of phloroglucinol was brominated in ether solution with 5 g of dioxane dibromide. After working up in the usual manner, 2.7 g of dibromophloroglucinol was obtained, m.p. 146 (from water).

8.550 mg substance: 4.763 mg Br (combustion in a stream of O_2). 5.300 mg substance: 2.965 mg Br, Found %: Br 55.70, 55.94, $C_6H_4O_3Br_2$. Calculated %: Br 56.29.

Bromination of 1-naphthol. 1.44 g of 1-naphthol in 20 ml of dioxane was brominated with 2.48 g of dioxane dibromide. 1.7 g (76%) of 4-bromo-1-naphthol was obtained; m.p. 112° (from aqueous methanol).

Bromination of 2-naphthol. 7.2 g of 2-naphthol was brominated in an analogous manner to 1-naphthol with 12.5 g of dioxane dibromide in dioxane solution. 10 g (90%) of 1-bromo-2-naphthol was obtained; m.p. 82° (from aqueous methanol).

Bromination of nerolin (2-methoxynaphthalene). 1.47 g of nerolin was brominated in dioxane solution with 2.5 g of dioxane dibromide. 2.3 g (97%) of 1-bromo-2-methoxynaphthalene was obtained; m.p. 83-84° (from aqueous methanol).

Bromination of 1-hydroxyanthraquinone. Several milliliters of dioxane were added to 2.24 g of 1-hydroxyanthraquinone and 2.5 g of dioxane dibromide, which had been carefully mixed together, and the mixture heated for 10 minutes to 50-60°. The mixture was poured into water, the precipitate filtered, and air dried. 2.99 g of 4-bromo-1-hydroxy-anthraquinone was obtained, m.p. 197° (from glacial acetic acid).

Bromination of 2-hydroxyanthraquinone. 2.24 g of 2-hydroxyanthraquinone was brominated in an analogous manner to 1-hydroxyanthraquinone with 2.5 g of dioxane dibromide. 2.8 g of 1-bromo-2-hydroxy-anthraquinone was obtained, m.p. 187° (from methanol).

Bromination of 1,2-dihydroxyanthraquinone (alizarin). 1.2 g of alizarin was carefully mixed with 1.25 g of dioxane dibromide and the mixture was heated to 50-60°, whereupon the color changed from orange-yellow to brown. The pasty mass obtained was worked up with sodium carbonate solution, acetic acid, and water, filtered, and air dried. Yield 1.6 g (100%); m.p. 264° (decomp.) (from aqueous acetic acid).

Bromination of salicylic acid. 6.9 g of salicylic acid mixed with 12.5 g of dioxane dibromide was heated to 70°. The colorless mixture was poured into water. 9.6 g of 4-bromosalicylic acid was obtained; m.p. 164-165° (from water.).

Bromination of 4-nitrophenol. 4.6 g of 4-nitrophenol was brominated in an anologous manner to salicylic acid with 8.3 g of dioxane dibromide. The mixture was poured into water, the precipitate separated and dissolved in methanol. A crystalline product was obtained by slowly evaporating the alcohol. 6 g (82%) of 2-bromo-4-nitrophenol was obtained; m.p. 112-114°.

SUMMARY

A new method is given for the bromination of phenols, naphthols, and hydroxyanthraquinones with the addition product of bromine and dioxane — dioxane dibromide.

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BROMINATION WITH DIOXANE DIBROMIDE

II. THE BROMINATION OF ALDEHYDES AND KETONES

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The direct bromination of aldehydes and ketones, as a rule, gives poor results, as the hydrogen bromide generated catalyzes the polymerization and condensation processes, especially for the aldehydes. The aldehydes are immediately changed by the action of acids into acidophobic compounds, such as the five membered heterocycles, pyrans and pyrroles. Ketones are much more stable to acids; however, many of them are strongly colored by the direct action of bromine. Because of this, there are no general and simple methods for brominating carbonyl compounds up to the present time.

All of the previous methods for the preparation of α-bromaldehydes do not start with the free aldehydes. The methods can be separated into two groups. The first group uses polymers of the aldehydes, such as paraldehyde. These trimers are brominated with bromine in carbon disulfide [1], or without solvents at low temperatures, −10-15° [2], and the bromo trimeric derivatives are depolymerized by heating to 140-160°. It must be pointed out, however, that the methods based upon the above principles nearly always give poor yields of the bromaldehydes (20-25%). The second group consists of methods which use monomers − aldehydes with protected carbonyl groups. The best worked out methods are those which use phosphorus trichlorodibromide, PCl_3Br_2, to brominate acetals [3]. A recently proposed method for the preparation of α-bromaldehydes uses enolacetates, which are reacted with bromine and then saponified [4]. The main fault of this group of methods is their length and many steps. Also, the yield of the final product leaves much to be desired. The yield does not exceed 40-45%, calculated on the aldehyde used.

As has been stated above, the direct bromination of ketones is possible. However, here the reaction is often complicated by a series of side reactions: oxidation, condensation, and polymerization. Many ketones can be advantageously brominated by a method worked out by A. E. Favorsky [5] in the presence of calcium carbonate. A rather good brominating agent for aliphatic ketones, starting with acetone, is PBr_5, as first shown by Favorsky[5]. Recently pyridinedibromide-hydrobromide [6] has been proposed as a brominating agent for ketones, especially those of the sterol series. N-bromsuccinimide [7] has also been used for the bromination of certain ketones.

In spite of the large number of proposed methods, not one of these can be used generally. Besides, the brominating agents are not always available, nor the method convenient, nor the yield of the bromoketone good.

In this report the results of the work on the use of dioxane dibromide as a brominating agent for aldehydes and ketones is given [8].

It was found that dioxane dibromide is an excellent brominating agent for both the aliphatic and alicyclic aldehydes and ketones. The bromination proceeds rather easily in the cold, and is not accompanied by polymerization or oxidation. The bromination may be made without solvents, but the best results are obtained in dioxane or ether solutions, especially in the latter. When the reaction is run in ether, very often two layers are formed in the reaction mixture. The upper, as the experiment showed, consisted of the bromaldehyde and the unreacted aldehyde in ether solution. The lower layer − a thick oil, which darkened in the air − is very soluble in water. The bromide ion is found in the aqueous solution. Upon making the aqueous solution basic, a distinct odor of dioxane is noticed. Apparently the lower layer is nothing more than a solution of hydrogen bromide in dioxane or, perhaps, even the unstable dioxanebromohydrin. This convenient separation of the hydrogen bromide from the reaction sphere results in a full protection of the aldehydes and ketones remaining in the ether from its harmful effects.

The yield of the brominated aldehydes and ketones in most cases is sufficiently high. Low yields were obtained for bromacetaldehyde (25-30%), phenylbromacetaldehyde (35-40%), and bromodecylaldehyde (20-25%); the latter was never obtained in an analytically pure state. However, the low yields did not arise from processes

occurring during the bromination, but from the inherent instability of the compounds themselves. Bromacetaldehyde, as is evident from the literature [9], rapidly polymerizes. Phenylbromacetaldehyde and bromodecylaldehyde decompose strongly on vacuum distillation, with the cleavage of HBr.

The proposed method was found especially convenient for alicyclic ketones which do not give good results with the other methods. This method was used in Acad. A. N. Nesmeyanov's laboratory for the bromination of spiro-4,5-decanon-6, 7-methylspiro-4,5-decanon-6, and 2,2,6-trimethylcyclohexanon-1; in all cases the corresponding α-bromoketones were obtained in high yields (50-80%).

The action of dioxane dibromide was studied on nine aldehydes: acetaldehyde, propionaldehyde, butyraldehyde, isobutyraldehyde, isovaleraldehyde, heptaldehyde, octylaldehyde, decylaldehyde, and phenylacetaldehyde; and on seven ketones: acetone, dipropyl ketone, diisopropyl ketone, cyclohexanone, menthone, acetophenone, and camphor.

It is interesting to point out that different types of camphor react differently with dioxane dibromide. For example: Japanese camphor starts reacting after the reaction mixture is heated for two minutes on the burner; native (Siberian) camphor reacts after several seconds of heating; while synthetic camphor only reacts after being heated for 10-15 minutes on the burner. However, camphor appears to be the only ketone among those studied which requires heating for the reaction.

EXPERIMENTAL

Bromination of acetaldehyde. 50 g of dioxane dibromide dissolved in ether was added dropwise at 5-10° to a solution of 8.8 g of acetaldehyde in 50 ml of ether. After the decolorization of the mixture, it was washed with a small amount of water, aqueous sodium carbonate, again with water, dried with anhydrous magnesium sulfate, the ether carefully removed, and the residue distilled. 7.5 g of bromacetaldehyde, b.p. 104-105°, n_D^{20} 1.4790, was obtained.

Bromination of propionaldehyde. 25 g of dioxane dibromide was added in small portions with shaking and water cooling to 5.8 g of the aldehyde dissolved in 25 ml of ether. The first portion of the reagent decolorized in 4-5 minutes, the later portions decolorized immediately. At the same time the solution darkened and separated into layers. At the end of the reaction, the lower layer was separated and the upper layer washed thoroughly with water, separated, and distilled. 7 g (51%) of the α-bromopropionaldehyde was obtained; b.p. 109-110°; n_D^{20} 1.4818.

Bromination of butyraldehyde. 50 g of dioxane dibromide was added with water cooling and stirring to 14.4 g of butyraldehyde. 2-3 minutes after addition of all of the reagent the mixture decolorized completely. The mixture was poured into water, the oil which separated taken up in ether, the ether layer washed and dried; after removal of the ether, the residue was vacuum distilled. 20.5 g of α-bromobutyraldehyde (68%) was obtained; b.p. 68-70° at 35-40 mm; n_D^{20} 1.4688.

Bromination of isobutyraldehyde. 7.2 g of isobutyraldehyde was brominated with 25 g of dioxane dibromide in ether solution. The decolorization of the reagent occurred very rapidly and the mixture separated into layers. After the usual workup, 9 g (58%) of α-bromoisobutyraldehyde was obtained; b.p. 112-113°; n_D^{20} 1.4530.

Bromination of isovaleraldehyde. 8.6 g of isovaleraldehyde was brominated in ether solution with 25 g of dioxane dibromide in the usual manner. 14 g (89%) of α-bromoisovaleraldehyde was obtained; m.p. 46-47° at 15 mm; n_D^{20} 1.4622.

Bromination of heptaldehyde. 25 g of dioxane dibromide was added in small portions, with water-cooling and shaking, to 11.4 g of freshly distilled heptaldehyde; after each addition, we waited until the reaction mixture was completely decolorized before adding the next portion of the reagent. At the beginning, a rapid decolorization occurred, the last portions of the reagent decolorized slowly. At the end of the reaction there was a slight darkening and a separation of layers. The lower layer was separated, the upper taken into ether, washed very thoroughly with water, and dried with anhydrous magnesium sulfate. The ether was evaporated in vacuo and the residue was then rapidly distilled in a stream of nitrogen. 12 g (62%) of α-bromoheptaldehyde was obtained: b.p. 78-80° at 10 mm; n_D^{20} 1.4650.

Bromination of octaldehyde. 12.8 g of freshly distilled n-octaldehyde was brominated in ether (25 ml) solution with 25 g of dioxane dibromide, the reagent being added stepwise with water cooling and shaking, and with waiting each time for the complete decolorization. At first the reagent decolorized slowly, then extremely

rapidly; the final portions of the reagent decolorized slowly. The mixture separated into layers. It was processed in the same way as heptaldehyde. 11.4 g (55%) of α-bromoctaldehyde was obtained; b.p. 110-111° at 23 mm; n_D^{20} 1.4650.

8.690 mg substance: 14.710 mg CO_2; 5.767 mg H_2O; 3.380 mg Br 5.380 mg substance: 9.130 mg CO_2; 3.825 mg H_2O; 2.235 mg Br. Found %: C 46.20, 46.31; H 7.43; Br 38.89, 38.80. $C_8H_{15}OBr$. Calculated %: C 46.17; H 7.27; Br 38.40.

This was the first preparation of α-bromoctaldehyde.

Bromination of decaldehyde. 15.6 g of freshly distilled n-decaldehyde was brominated with 25 g of dioxane dibromide in ether solution in the same manner as for n-octaldehyde. After processing it in the usual manner, the ether was evaporated in vacuum and the residue vacuum-distilled in a stream of nitrogen. In spite of all precautions, a strong decomposition took place during the distillation with the separation of HBr. A fraction collected at 120-130° at 14-16 mm, yellowish brown in color, was redistilled. On redistillation a decomposition and separation of HBr again occurred. 5 g of a light yellow liquid with lachrymatory properties was obtained, b.p. 128-130° at 15 mm; the liquid darkened rapidly. The bromodecaldehyde could not be obtained in an analytically pure state. The action of phenylhydrazine on either an alcohol or ether solution of the brominated aldehyde produced the cleavage of hydrogen bromide and the formation of phenylhydrazine hydrobromide, with separation of a thick oil, which did not have lachrymatory properties and contained no bromine. The action of sodium bisulfite on the brominated aldehyde did not lead to the formation of a definite product.

Bromination of phenylacetaldehyde. 12 g of freshly distilled phenylacetaldehyde was brominated in the usual manner in an ether solution. After the standard work up, the bromaldehyde obtained was vacuum-distilled in a stream of nitrogen. 8 g (40%) of phenylbromacetaldehyde was obtained; b.p. 112-114° at 15 mm; n_D^{20} 1.5916.

Bromination of acetone*. 11.6 g of acetone was brominated in ether solution with 50 g of dioxane dibromide, with shaking and water cooling. The colorless solution was well washed with water, sodium carbonate solution, again with water, and dried with anhydrous magnesium sulfate. After the removal of the ether, the residue was vacuum-distilled in a stream of nitrogen. 22.8 g (83%) of bromacetone was obtained; b.p. 44-46° at 15 mm. The whole process must be carried out the same day, without postponing the distillation, or the yield drops sharply.

Bromination of dipropyl ketone. 25 g of dioxane dibromide was slowly added to 11.7 g of dipropyl ketone. A rapid decolorization and a slight warming of the reaction mixture occurred. The reaction mixture was poured into water and the oil which separated taken into ether, washed, dried, and distilled. 15 g (76%) of the bromoketone was obtained; b.p. 78-80° at 15 mm.

Bromination of diisopropyl ketone. 25 g of dioxane dibromide was added in small portions to 11.2 g of diisopropyl ketone dissolved in 10 ml of dioxane. Within 2-3 minutes after the addition of all the reagent, the mixture decolorized. The solution was poured into water, the oil separated, dried, and vacuum-distilled. 15 g (78%) of the bromodiisopropyl ketone was obtained: b.p. 152-153° at 11 mm; n_D^{20} 1.4512.

Bromination of menthone. 8 g of menthone was brominated in a dioxane solution in analogous fashion, with 13 g of dioxane dibromide. After the usual processing, it was vacuum-distilled in a stream of nitrogen. 7 g (59%) of bromomenthone was obtained; b.p. 102-105° at 14 mm.

Bromination of cyclohexanone. 10 g of cyclohexanone was brominated in a dioxane-ether mixture (10 ml + 50 ml) with 25 g of dioxane dibromide. The mixture was thoroughly washed with water, dried, and vacuum-distilled in a stream of nitrogen. 11 g (60%) of bromocyclohexanone was obtained; b.p. 114-116° at 32 mm.

Bromination of acetophenone. 11 g of acetophenone was brominated in dioxane solution with 25 g of dioxane dibromide. The mixture was poured into water, the oil taken up into ether, dried and the ether evaporated.

* It must be pointed out that if the acetone contains alcohol or other contaminants, the start of the reaction is delayed. In this case it is desirable to add a drop of conc. hydrochloric acid to the mixture, and to warm it up slowly. As soon as the first portion of the reagent is decolorized, the subsequent portions are decolorized immediately.

The residue crystallized on standing. 18 g (95%) of ω-bromacetophenone was obtained; m.p. 50° (from aqueous methanol).

Bromination of camphor. 4.5 g of Japanese d-camphor was mixed with 7.5 g of dioxane dibromide and and heated for 2-3 minutes on the burner. The mixture decolorized with the separation of HBr. It was poured into water; the oil which separated crystallized rapidly. The crystals were sucked off and air dried. 5.6 g (80%) of d-bromocamphor was obtained, m.p. 74° (before recrystallization), 75° (from aqueous alcohol).

SUMMARY

A new method of brominating aldehydes and ketones by means of dioxane dibromide is given.

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STERIC HINDRANCES IN ORGANO-MAGNESIUM REACTIONS

XIV. AN UNUSUAL REACTION BETWEEN α-MONOCHLOROETHERS AND ARYL MAGNESIUM HALIDES

I. I. Lapkin and O. M. Lapkina

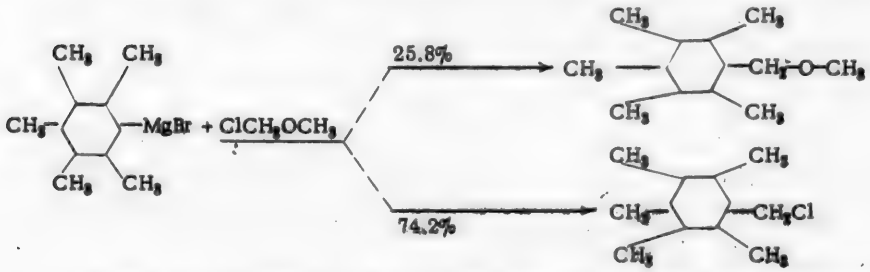
In a previous communication [1], it was shown the reaction of aryl magnesium halides with monochloromethylalkyl ethers, in relation to the degree of orthosubstitution of the phenyl radical by the alkyl groups, leads to different results. Unsubstituted and orthomonosubstituted aryl magnesium halides, as well as naphthyl magnesium halides, react normally with the above ethers to give the corresponding ether. When orthodisubstituted aryl magnesium halides react with the same monochloromethylalkyl ethers, the character of the reaction changes and the main product of the reaction is not the corresponding ether, but the orthodisbustituted benzyl chloride.

In the same report it was stated that the reason for this reaction path lies in the fact that, in the presence of the ortho effect on phenyl radicals, the sterically more accessible, although less reactive, alkoxy group of the chloroether reacts, instead of the more reactive chloromethyl group.

In order to confirm the unusual reaction between the above substances, two more reactions, the reaction of duryl magnesium bromide and monochloromethylethyl ether and the reaction between pentamethylphenyl magnesium bromide and monochlorodimethyl ether, were studied.

The first reaction, under the conditions used (Expt. 1), led to the formation of the following products:

The second reaction under analogous conditions (Expt. 2) gave the following products:



In order to be satisfied that the conclusion given on the reasons for the unusualness of the above reaction was correct, it was necessary to examine all variations in the mechanism of this anomaly.

First of all it was necessary to examine the possibility of the formation of the orthodisubstituted benzyl chlorides as a consequence of the easy hydrolysis of α-chloroethers. The HCl formed on hydrolysis could have split the benzylalkyl ether — the normal reaction product — forming, in this way, the benzyl chloride.

$$R\text{-}CH_2\text{-}O\text{-}CH_3 + HCl \longrightarrow R\text{-}CH_2OH + CH_3Cl;\ R\text{-}CH_2OH + HCl \longrightarrow R\text{-}CH_2Cl + H_2O.$$

TABLE 1

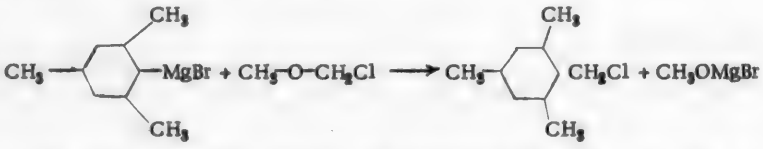
Reaction components (ratio 1:1)	Duration of heating, in hours	Composition of the reaction product (in %)	
		2,4,6-Trimethylbenzylmethyl ether (by calculation)	2,4,6-Trimethylbenzyl chloride
1. Mesityl magnesium bromide + monochloromethyl ether	1	38.0	62.0
2. Ditto	3	42.1	57.9
3. Ditto	5	45.2	54.8

TABLE 2

Reaction components	Ratio of the reaction components	Composition of the reaction product (in %)	
		2,4,6-Trimethylbenzylmethyl ether (by calculation)	2,4,6-Trimethylbenzyl chloride
1. Mesityl magnesium bromide + monochloromethyl ether	1:0.75	49.5	50.5
2. Ditto	1:1	38.2	61.8
3. Ditto	1:1.25	30.7	69.3

This equivalent variation of the reaction mechanism, however, had to be excluded because: first, the reaction was run under conditions which prevented the entrance of moisture into the flask; secondly, if the formation of the benzyl chlorides depended on the hydrolysis of the monochloromethylalkyl ethers, then it should have been formed in the case of the orthomonosubstituted benzylalkyl ethers, which, however, as the experiment proved, did not occur. Besides, if the process which formed the benzyl chloride was a secondary process, then an increase of the heating period would have increased the amount of the benzyl chloride in the reaction mixture, which actually, did not happen. Special experiments proved that increasing the heating period of the reaction mixture was not accompanied by an increase in the amount of benzyl chloride in the reaction products, but, on the contrary, in a decrease (Expt. 3) (Table 1).

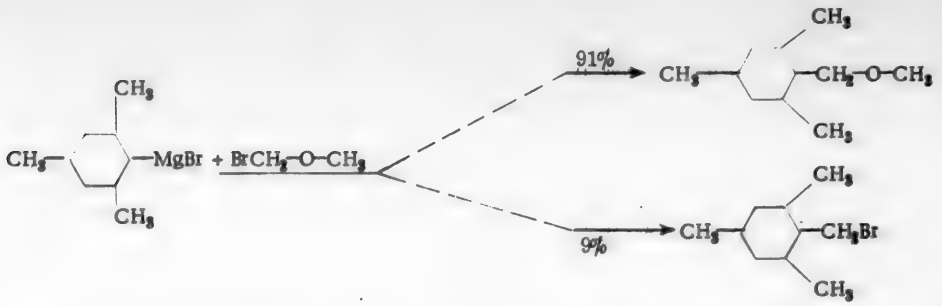
This decrease may be explained by the fact that the second product of the reaction forming the orthodisubstituted benzyl chloride as in the following equation:



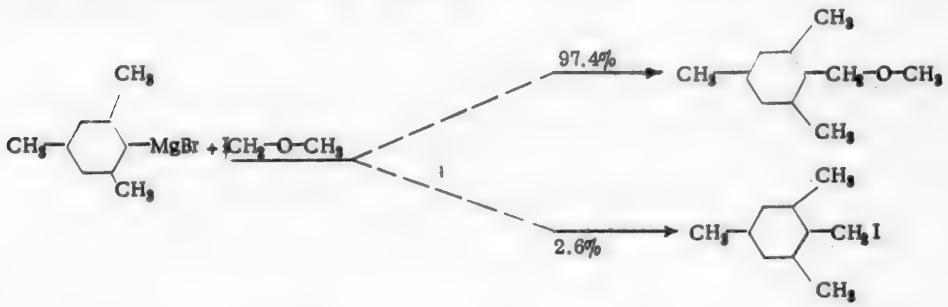
appears to be the alkoxy magnesium bromide, the subsequent reaction of which with the first product, is the reason for the formation of a certain amount of the benzylalkyl ether. From this fact it also follows that if the reaction is run with an excess of monochloromethyl ether, which reacts more rapidly with the alkoxy magnesium bromides, then the yield of the product ought to increase. There should also be an increase in the amount of benzyl chloride in the total products. The experiment confirmed this exactly. When the amount of the chloroether was increased, the amount of the product and the amount of benzyl chloride in it was increased (Expt. 3) (Table 2).

Finally, experiments were made to determine the degree of stability of the orthosubstituted benzylmethyl ethers to the action of monochloromethylethyl ether. Extremely interesting results are obtained on comparing the action of monochloromethyl ether on the orthodisubstituted aryl magnesium halides with that of monobromo- and monoiodomethyl ether. As it is known, monobromo- and monoiodomethyl ethers are both more active chemically than monochloromethyl ether, and monoiodomethyl is more active than monobromomethyl ether. This increase in chemical activity of the bromo- and iodoethers overcomes the steric hinderance of the alkyl orthosubstituents and because of this, the reaction between the orthodisubstituted aryl magnesium halides and the above haloethers has a different character.

The main reaction product from the reaction of monobromomethyl ether with mesityl magnesium bromide appears to be methyl-2,4,6-trimethylbenzyl ether. The second reaction product, 2,4,6-trimethylbenzylbromide is obtained in insignificant quantity (Expt. 4).



Monoiodomethyl ether reacts even more actively with mesityl magnesium bromide. The main product of the reaction appears to be methyl-2,4,6-trimethylbenzyl ether, the amount of 2,4,6-trimethylbenzyl iodide in the reaction product is even less. (Expt. 5).



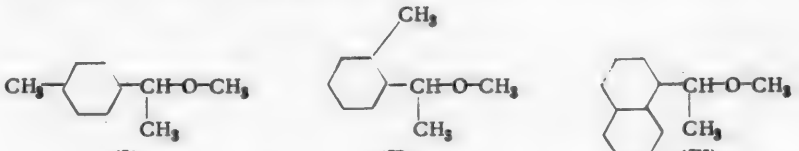
These facts also support the conclusion that the reason for the anomalous course of the reaction studied lies in the unequal steric accessibility of groups, and that the synthesis of the orthodisubstituted benzyl chlorides is not a result of secondary processes (hydrolysis, terminal cleavage), because these processes are more pronounced for monobromo- and monoiodomethyl ethers, and the reaction with these substances takes a normal course with the formation of ethers.

There is a considerable interest in the study of the reaction between the same organo-magnesium compound and other chloro ethers, namely the α-chloroethylalkyl ethers. A comparison of the activity of the α-halide found in the chloromethylalkyl ethers and in α-chloroethylalkyl ethers, shows that the halide in the latter has a greater degree of activity than in the former. For this reason the α-haloethylalkyl ethers which contain a halogen atom attached to secondary carbon react more readily than the halomethyl alkyl ethers in which this atom is found attached to a primary carbon atom.

The orthomonosubstituted and unsubstituted aryl magnesium halides react with α-monochloroethylalkyl ethers, as was expected, mainly in the direction of the formation of ethers.

1-Methyl-4-(α-methoxyethyl)benzene (I) is formed by the reaction of p-tolyl magnesium bromide with α-chloroethylmethyl ether (Expt. 6). A similar product, 1-methyl-2-(α-methoxyethyl)benzene (II) is formed by the reaction between α-monochloroethylmethyl ether and o-tolyl magnesium bromide (Expt. 7).

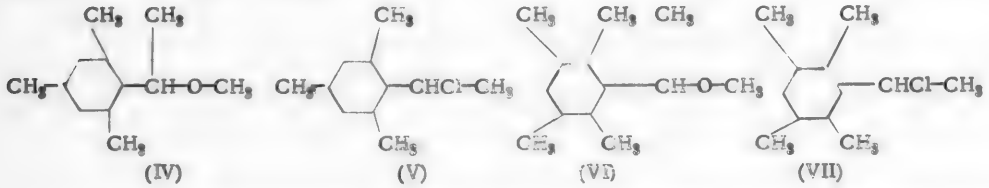
α-Naphthyl magnesium bromide also reacts normally with the above ether, i.e. with the formation of 1-(α-methoxyethyl) naphthalene (III) (Expt. 8).



Of the two possible directions for the reaction with orthodisubstituted aryl magnesium halide which (the directions) were discussed above, the first proved to be the main one. The main products of the reaction were,

as in the case of the orthomonosubstituted, the ethers. The second of the above directions only occurs to an almost insignificant degree. 1,3,5-trimethyl-6-(α-methoxyethyl)-benzene (IV) is formed by the reaction of mesityl magnesium bromide with α-monochloroethylmethyl ether (Expt. 9). The product of the second direction of the reaction, 1,3,5-trimethyl-6-(α-chloroethyl)-benzene (V) is formed in an almost insignificant amount (5.3%).

Duryl magnesium bromide reacts similarly to mesityl magnesium bromide, the reaction of which with the same α-monochloroethylmethyl ether leads to the formation of 1,2,4,5-tetramethyl-6-(α-methoxyethyl)-benzene (VI) (Expt. 9). The second product of the reaction, 1,2,4,5-tetramethyl-6-(α-chloroethyl)-benzene (VII), was also obtained in a very small amount (4.7%).

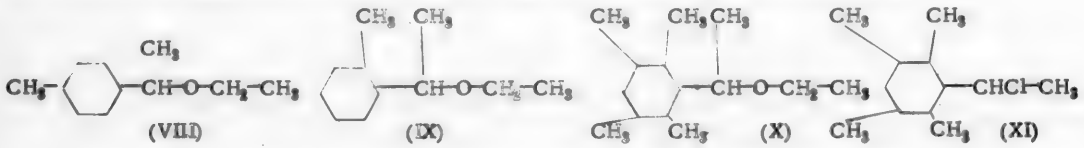


(IV) (V) (VI) (VII)

The second representative of the α-chloroethylalkyl ether group, namely, α-monochlorodiethyl ether, differs little in its chemical properties from α-monochloroethylmethyl ether. This difference lies only in its still greater thermal instability as compared to α-monochloroethylmethyl ether. The reaction characteristics of these ethers with organo-magnesium compounds are therefore the same. 1-Methyl-4-(α-ethoxyethyl)-benzene (VIII) is formed as the only product of the reaction of p-tolyl magnesium bromide with α-monochlorodiethyl ether (Expt. 10).

The only product of the reaction of o-tolyl magnesium bromide with α-monochlorodiethyl ether is 1-methyl-2-(α-ethoxyethyl)-benzene (IX) (Expt. 11).

Finally, duryl magnesium bromide, reacting with the same chloroether, forms 1,2,4,5-tetramethyl-6-(α-ethoxyethyl)-benzene(X) as the main reaction product (Expt. 12). The amount of the secondary reaction product, 1,2,4,5-tetramethyl-6-(α-chloroethyl)-benzene (XI) is almost insignificant (3.5%).



(VIII) (IX) (X) (XI)

Returning once more to the question of the reasons for the unusual reaction between orthodisubstituted aryl magnesium halides and chloromethyl ethers, it must be emphasized that the explanation that the reason for the anomalous direction of the reaction is steric in character is upheld by the fact that the reaction between the same organo-magnesium compounds and the chloroethylalkyl ethers is normal in character. If the formation of the benzyl chlorides was a result of secondary processes, then, on the strength of the chemical and thermal instability of the chloroethers, these processes should have taken place to a greater extent with the α-chloroethylalkyl ethers than with the chloromethyl alkyl ethers because the former are less stable chemically and thermally than the latter.

EXPERIMENTAL

The usual conditions for the reaction between the aryl magnesium bromides and the chloromethylalkyl ethers were: A solution of the aryl magnesium bromide in ether (3 volumes) was added slowly, with mechanical stirring and cooling of the reaction flask in ice water, to a solution of the chloromethylalkyl ether in three volumes of absolute ether. This order of addition was used for the orthodisubstituted aryl magnesium bromide because with the reverse, the benzyl chloride which forms then reacts with the residual magnesium, leading to the formation of symmetrical arylethane hydrocarbons. This and the opposite (usual) order of addition can be used with orthomonosubstituted aryl magnesium halides because in both cases only ethers are formed. After the mixing of the reaction components, the mixture was heated for a certain time (usually one hour), and then decomposed with water with cooling. The ether layer was washed in a separatory funnel first with water, then with a 10% sodium bicarbonate solution, and again three times with water. After drying the ether with fused

sodium sulfate, the ether was distilled, the reaction product was redistilled in vacuo, and then analyzed.

1. Reaction of duryl magnesium bromide with monochloromethylethyl ether. Duryl bromide normally only reacts with magnesium in the presence of some low molecular weight alkyl halide, particularly ethyl bromide [2,3], so that the following starting materials were used: 35.5 g (1/6 mole) duryl bromide, 18.2 g (1/6 mole) of ethyl bromide, 10 g of magnesium, and 32 g (1/3 mole) of monochloromethylethyl ether. The reaction was run according to the above conditions. The reaction was run according to the above conditions. The reaction products were vacuum distilled at 12 mm: Fraction I—to 115°; Fraction II from 115-145° —19 g, the residue, 1.5 g. The second fraction was analyzed to determine the amount of 2,3,5,6-tetramethylbenzyl chloride in it (by heating a weighed amount of the product with a saturated alcoholic solution of silver nitrate and then analyzing the silver chloride [4] and ethyl-2,3,5,6-tetramethylbenzyl ether formed).

0.1341 g substance: 0.0759 g AgCl. Found %: Cl 14.0. 0.1128 g substance: 0.0265 g AgI. Found %: OC_2H_5 4.5.

These figures can be used to show that Fraction II contained 72.0% of 2,3,5,6-tetramethylbenzyl chloride and 19.1% of ethyl-2,3,5,6-tetramethylbenzyl ether. On calculating for a pure mixture of the chloride and the ether, these figures corresponded to 79 and 21%.

Because the second fraction crystallized very rapidly after redistillation, the crystals of 2,3,5,6-tetramethylbenzyl chloride were filtered off on a Buchner funnel from the liquid part, and purified by recrystallization from petroleum ether. M.p. 85-86°.

0.1134 g substance: 0.0851 g AgCl. Found %: Cl 18.56. $C_{11}H_{15}Cl$. Calculated %: Cl 19.12.

Upon heating with sodium ethylate, the above chloride was changed to ethyl-2,3,5,6-tetramethylbenzyl ether (not listed in the literature).

B.p. 121-122° (8 mm).

0.1226 g substance: 0.3639 g CO_2; 0.1120 g H_2O. Found %: C 81.00; H 10.22. $C_{13}H_{20}O$. Calculated %: C 81.19; H 10.49.

2. Reaction of pentamethylphenyl magnesium bromide with monochloromethylether. Pentamethylphenyl bromide, like duryl bromide, only reacts with magnesium in the presence of ethyl bromide so that the following were used to run the reaction: 45 g (0.2 mole) pentamethylphenyl bromide, 21.8 g (0.2 mole) ethyl bromide, 12 g magnesium, and 32.2 g (0.4 mole) monochloromethyl ether. The reaction mixture was heated for one hour. The following fractions were obtained on vacuum distillation.

Fraction I, to 120° (7 mm) —11.4 g; Fraction II, 120-155° (7 mm) —19.0 g; residue —2.0 g.

For determination of the amount of pentamethylbenzyl chloride in the second fraction, a weighed amount was heated with a portion of an alcoholic solution of silver nitrate.

0.1244 g substance: 0.0648 g AgCl. Found %: Cl 12.88.

The amount of pentamethylbenzyl chloride in the fraction was 71.4%.

A quantitative determination of the methyl group showed the amount of methylpentamethylbenzyl ether in the fraction;

0.1181 g substance: 0.0358 g AgI. Found %: OCH_3 4.0.

This corresponds to 24.8% of methylpentamethylbenzyl ether in the fraction. By recalculating for a pure mixture of the chloride and the ether, these figures will be 74.2 and 25.8%.

To change the above chloride into the ether, the second fraction was worked up with sodium methylate in a methyl alcohol solution by heating for 15 minutes. The methylpentamethylbenzyl ether obtained had a b.p. 128-130° at 7 mm. M.p. 44° (from petroleum ether). This ether is not listed in the literature.

0.1204 g substance: 0.3575 g CO_2; 0.1114 g H_2O. 0.1289 g substance: 0.1483 g AgI. Found %: C 81.04; H 10.35; OCH_3 15.2. $C_{13}H_{20}O$. Calculated %: C 81.25; H 10.41; OCH_3 16.1.

3. Reaction of mesityl magnesium bromide and monochloromethyl ether. a) The influence of prolonged heating. In order to answer the question of the change of the composition of the product and its quantitative yield upon lengthening the heating time of the reaction mixture, three extra experiments were made under almost

identical conditions. Only the heating time was varied, from 1-5 hours. The reactants (mesityl magnesium bromide and monochloromethyl ether) were taken in 1/7 mole quantities. The main fractions were taken at 95-115° at 6 mm, and were analyzed for the amount of 2,4,6-trimethylbenzyl chloride in them [4]. The weight of the main fractions was from 13.7-14.0 g. The results are listed in Table 1.

This data indicates that when the heating time of the reaction mixture is increased the quantitative yield of the product stays the same, although the 2,4,6-trimethylbenzyl chloride content decreases somewhat.

b) Influence of variation in the ratio of the reactants. In order to answer this question three experiments were made once more. An ether solution of mesityl magnesium bromide prepared from 120 g of mesityl bromide was divided into three equal parts (of 0.2 mole) and each part was then added separately to three different weights of monochloromethyl ether, (12.1, 16.1, and 20.1 g), dissolved in absolute ether. The reaction mixture was then heated for one hour. The main fractions were taken at 95-115° at 6 mm, and analyzed for the amount of 2,4,6-trimethyl-benzyl chloride in them [4]. The weight of the main fraction in the first experiment was 16.2 g, in the second 18.0 g, and in the third 20.1 g. The amount of 2,4,6-trimethylbenzyl chloride in the main fractions is listed in Table 2.

The results of these experiments indicate that when the amount of monochloromethyl ether is increased, the yield of the product, as well as the amount of 2,4,6-trimethylbenzyl chloride in it, is increased.

c) Determination of the comparative stability of orthosubstituted methylbenzyl ethers to the action of monochlorodimethyl ether. Methyl-2-methylbenzyl and methyl-2,4,6-trimethylbenzyl ethers in 10 g quantities dissolved in ether (3 volumes) were used in the determination of the comparative stability of ortho mono- and disubstituted methyl benzyl ethers to the action of monochlorodimethyl ether. These ethers were heated for 3 hours with a quantity (7 g) of monochlorodimethyl ether. Water was then added to the reaction mixture and the ether layer was washed with a sodium carbonate solution and again with water. After drying the ether solution, the solvent was distilled and the residue was vacuum distilled (wherein the boiling point of the ether almost did not change) and analyzed for chloride.

On heating methyl-2-methylbenzyl ether with the above chloroether, 0.24% of 2-methylbenzyl chloride was formed.

0.5013 g substance: 0.0013 g AgCl. Found %: Cl 0.06.

On heating methyl-2,4,6-trimethylbenzyl ether with the same chloroether, 3.5% of 2,4,6-trimethylbenzyl chloride was formed.

0.5247 g substance: 0.0156 g AgCl. Found %: Cl 0.74.

Similar results are obtained on heating the above substance in the presence of $MgCl_2$ (3 g).

4. Reaction of mesityl magnesium bromide with monobromodimethyl ether. The method of Hamonet [5], employing the reaction of gaseous HBr with monochlorodimethyl ether, was used to prepare monobromodimethyl ether.

$$CH_2Cl{-}O{-}CH_3 + HBr \longrightarrow CH_2Br{-}O{-}CH_3 + HCl.$$

HBr was passed in until saturation into the chloroether, and the monobromodimethyl ether which formed was redistilled from the flask through a dephlegmator. B.p. 86-87°.

40 g (0.2 mole) of mesityl bromide, 6 g of magnesium, and 25 g (0.2 mole) of monobromodimethyl ether were used for the experiment. An ether solution of the organo-magnesium compound was added to the monobromodimethyl ether. The reaction mixture was heated for one hour. Fraction 1, to 87° (6 mm); Fraction 2, 87-140° (6 mm); −22 g; residue 1.5 g.

The subsequent analysis of the second fraction was done in the previously given manner.

0.1171 g substance: 0.0084 g AgBr. Found %: Br 3.05. 0.1311 g substance: 0.1581 g AgI. Found %: OCH_3 15.9.

Therefore the second fraction contains 8.3% of 2,4,6-trimethylbenzyl bromide and 84.2% of methyl-2,4,6-trimethylbenzyl ether. On recalculation for a pure mixture, these figures equal 9 and 91%.

After purification of the second fraction by heating with sodium methylate, followed by rectification,

methyl-2,4,6-trimethylbenzyl ether with b.p. 95-97° (7 mm) was obtained. In the literature [7], b.p. 109-110° at 15 mm is given for this compound. Yield 13.5 g (40%).

0.1215 g substance: 0.1601 g AgI. Found %: OCH_3 17.4. $C_{11}H_{16}O$. Calculated %: OCH_3 18.9.

5. Reaction of mesityl magnesium bromide with monoiodomethyl ether. For the preparation of monoiodomethyl ether, Henry [6] recommends that a mixture of formalin and methyl alcohol be saturated with gaseous HI. As this procedure was not very convenient technically, another procedure based upon the reaction of KI with monochloromethyl ether was used.

Well-dried and pulverized potassium iodide was placed into a flask provided with a reflux condenser. While the flask was cooled in an ice-salt mixture, the monochlorodimethyl ether was slowly added to it. To complete the reaction, the reaction flask was heated on the water bath for one hour. Because monoiodomethyl ether is so thermally unstable and decomposes completely into methyl iodide and polyoxymethylene for purification it was vacuum distilled. B.p. 39° at 20 mm.

40 g (0.2 mole) of mesityl bromide, 6 g of magnesium, and 34.4 g (0.2 mole) of monoiodomethyl ether were used for the reaction of mesityl magnesium bromide and monoiodomethyl ether. The ether solution of mesityl magnesium bromide was separated from the residual magnesium and added to the monoiodomethyl ether. The reaction mixture was heated for a period of one hour. Fraction I, to 92° (9 mm), Fraction II, 92-155° (9 mm) —24.0 g; residue —1.5 g.

The second fraction contained the iodide and the ether, whose quantities were determined by the earlier-given methods.

0.1238 g substance: 0.0021 g AgI. Found %: I 0.92. 0.1361 g substance: 0.1711 g AgI. Found %: OCH_3 16.6.

These figures indicate the following quantitative composition for the above substances in Fraction II: 2,4,6-trimethylbenzyl iodide 2.3% and methyl-2,4,6-trimethylbenzyl ether 87.8%. On calculating for a pure mixture, these figures are equal to 2.6 and 97.4%. After purification of Fraction II with sodium methylate, followed by rectification, methyl-2,4,6-trimethylbenzyl ether, b.p. 92-93° (5 mm) was obtained.

0.1197 g substance: 0.1632 g AgI. Found %: OCH_3 18.0. $C_{11}H_{16}O$. Calculated %: OCH_3 18.9.

6. Reaction of p-tolyl magnesium bromide with α-chloroethylmethyl ether. 42.8 g (0.25 mole) of p-bromotoluene, 7 g of magnesium, and 23.6 g (0.25 mole) of α-monochloroethylmethyl ether were used for the experiment. The conditions given above were used for the reaction. For this group of experiments only one order of addition of the reaction components were used: the ether solution of the organo-magnesium compound decanted from the residual magnesium was added to an ether solution of the chloroether. After mixing the reaction components, the reaction mixture was heated for one hour and then decomposed with water, with cooling, and, if the ether layer remained cloudy, with 10% acetic acid. The mixture was transferred to a separatory funnel, the lower aqueous layer was separated, the ether layer was washed first with a 5% solution of sodium bicarbonate, and then three times with water.

Since benzyl chlorides, and especially those containing a chlorine on a secondary carbon atom, are prone to hydrolysis, the possibility of this occurring was tested by determining the hydroxyl groups in the reaction product by Chugaev's method. The above method of washing the ether layer was not used until it was established that no appreciable hydrolysis occurred.

After the ether solution was dried with fused sodium sulfate, the ether was distilled, the reaction product fractionated and then analyzed. Fraction I, to 70° (9 mm); Fraction II, 70-100° (9 mm) —18.0 g; Fraction III, 100-150° (9 mm) —4.0 g; residue —1.5 g.

Because no silver chloride could be obtained on treating Fraction II with alcoholic silver nitrate, showing that no noticeable amount of 1-methyl-4-(α-chloroethyhl)-benzene was present, Fraction II was refractionated, resulting in the separation of 1-methyl-4-(α-methoxyethyl)-benzene, b.p. 72-73° at 8 mm. Yield 14 g (38%). A final purification of this ether by heating with sodium methylate in a methyl alcohol solution did not change the boiling point. This ether is not listed in the literature.

n_D^{20} 1.4930; d_4^{20} 0.9300; MR_D 46.94; calculated 46.42.

0.1019 g substance: 0.2978 g CO_2; 0.0858 g H_2O. 0.1490 g substance: 0.2110 g AgI. Found %: C 79.75; H 9.42; OCH_3 18.71. $C_{10}H_{14}O$. Calculated %: C 79.95; H 9.39; OCH_3 20.65.

Fraction III (100-150° at 9 mm) was dissolved in ethyl alcohol and cooled. The crystals of di-p-tolyl which separated melted at 121° after purification by twofold recrystallization. The literature [8] gives m.p. 120° for di-p-tolyl.

0.1299 g substance: 0.4385 g CO_2; 0.0907 g H_2O. Found %: C 92.11; H 7.81. $C_{14}H_{14}$. Calculated %: C 92.26; H 7.74.

7. Reaction of o-tolyl magnesium bromide with α-monochloroethylmethyl ether. 34.2 g (0.2 mole) o-bromotoluene, 6 g of magnesium, and 18.9 g (0.2 mole) of α-monochloroethylmethyl ether were used for the reaction. The usual reaction conditions given above were used. Fractionation of the product obtained gave the following results: Fraction I, to 82° (20 mm); Fraction II, 82-95° (20 mm) –14.6 g; residue –1.5 g.

For the determination of the amount of 1-methyl-2-(α-chloroethyl) benzene in the second fraction, a weighed amount was heated with an alcoholic silver nitrate solution.

0.4202 g substance: 0.0043 g AgCl. Found %: Cl 0.25. The amount of 1-methyl-2- (α-chloroethyl)-benzene in the substance is equal to 1.1%.

The remainder of Fraction II was then heated with sodium methylate dissolved in methyl alcohol in order to convert the 1-methyl-2-(α-chloroethyl)-benzene present to 1-methyl-2-(α-methoxyethyl)-benzene. After a final fractionation of the purified substance, 1-methyl-2-(α-methoxyethyl)-benzene, b.p. 90-91° at 25 mm, was isolated. Yield 12 g (40%). This ether is not listed in the literature.

n_D^{20} 1.4989; d_4^{20} 0.9433; MR_D 46.71; calculated 46.42.

0.1338 g substance: 0.3909 g CO_2; 0.1124 g H_2O. 0.1634 g substance: 0.2398 g AgI. Found %: C 79.72; H 9.40; OCH_3 19.38. $C_{10}H_{14}O$. Calculated %: C 79.95; H 9.39; OCH_3 20.65.

8. Reaction of α-naphthyl magnesium bromide with α-monochloroethylmethyl ether. Starting materials: 69 g (1/3 mole) of α-bromonaphthalene, 9 g magnesium, and 31.5 g (1/3 mole) of α-monochloroethylmethyl ether.

The usual reaction conditions were used. Fraction I, to 125° (13 mm); Fraction II, 125-145° (13 mm) –45.0 g; residue –3.0 g.

Silver chloride did not separate when a weighed amount of Fraction II was heated with alcoholic silver nitrate, which indicated that 1-(α-chloroethyl)-naphthalene was not present in the reaction product. On a further fractionation of the second fraction, 1-(α-methoxyethyl)-naphthalene, b.p. 109-110° at 3 mm, was isolated. Yield 31 g (50%). A final purification of the ether by heating it for 10 minutes with sodium methylate in methyl alcohol solution did not change the boiling point. This ether is not listed in the literature.

n_D^{20} 1.5931; d_4^{20} 1.0490; MR_D 60.61; calculated 57.14 (ME 3.47).

0.2190 g substance: 0.6744 g CO_2; 0.1458 g H_2O. 0.5308 g substance: 0.6558 g AgI. Found %: C 84.03; H 7.45; OCH_3 16.33. $C_{12}H_{16}O$. Calculated %: C 83.83; H 7.58; OCH_3 16.66.

9. Reaction of mesityl magnesium bromide with α-monochloroethylmethyl ether. 50.0 g (0.25 mole) mesityl bromide, 7 g of magnesium, and 23.6 g (0.25 mole) of α-monochloroethylmethyl ether were used. The usual reaction conditions were used.

Fraction I, to 80° (6 mm); Fraction II, 83-120° (6 mm); 20.2 g; residue –2.0 g.

For determination of the amount of 1,3,5-trimethyl-6-(α-chloroethyl) benzene in the second fraction, a weighed amount was heated, as usual, for 15 minutes with an alcoholic silver nitrate solution.

0.4122 g substance: 0.0176 g AgCl. Found %: Cl 1.05. The amount of 1,3,5-trimethyl-6-(α-chloroethyl)-benzene in the reaction product corresponds to 5.3 %.

In order to transform the above chloride in the product in the remainder of Fraction II to 1,3,5-trimethyl-6-(α-methoxyethyl)-benzene, it was heated with sodium methylate in methyl alcohol. The 1,3,5-trimethyl-6-(α-methoxyethyl)-benzene which was isolated from the final fractionation of the product purified with sodium methylate had b.p. 92-94° at 7 mm.

n_D^{20} 1.5052; d_4^{20} 0.9451; MR_D 55.96; calculated 55.66.

0.1574 g substance: 0.4642 g CO_2; 0.1418 g H_2O. 0.2898 g substance: 0.3466 g AgI. Found %: C 80.43; H 10.08; OCH_3 15.80. $C_{12}H_{18}O$. Calculated %: C 80.84; H 10.17; OCH_3 17.30.

This ether is not listed in the literature.

10. Reaction of duryl magnesium bromide with α-monochloroethylmethyl ether. Starting materials: 35.5 g (1/6 mole) duryl bromide, 18.1 g (1/6 mole) of ethyl bromide, 11 g of magnesium, and 31.5 g (1/3 mole) of α-monochloroethylmethyl ether.

The usual reaction conditions were used for the reaction studied. Fraction I, to 97° (7 mm); Fraction II, 97-130°, –15.0 g; residue –2.0 g.

The second fraction contains an insignificant amount of the second reaction product, 1,2,4,5-tetramethyl-6-(α-chloroethyl)-benzene.

0.3843 g substance: 0.01351 g AgCl. Found %: Cl 0.87.

The amount of the above chloride in the reaction product corresponds to 4.7%.

In order to make the whole reaction product more homogeneous, Fraction II was heated with sodium methylate in methyl alcohol. The 1,2,4,5-tetramethyl-6-(α-methoxyethyl)-benzene isolated after a final recrystallization from alcohol had m.p. 109-110°. There is no report of this ether in the chemical literature.

0.1102 g substance: 0.3272 g CO_2; 0.1032 g H_2O. 0.1524 g substance: 0.1642 g AgI. Found %: C 80.97; H 10.47; OCH_3 14.23. $C_{13}H_{20}O$. Calculated %: C 81.19; H 10.48; OCH_3 16.91.

11. Reaction of p-tolyl magnesium bromide with α-monochlorodiethyl ether. 43 g (0.25 mole) of p-bromotoluene, 7 g of magnesium, and 27.1 g (0.25 mole) of α-monochlorodiethyl ether were used for the reaction.

Fractionation of the mixture of substances obtained gave the following results: Fraction I, to 75° (12 mm); Fraction II, 75-110°. (12 mm) –21.5 g; residue 3.5 g.

Heating a weighed amount of Fraction II with an alcoholic silver nitrate solution did not produce any silver chloride, showing the absence of 1-methyl-4-(α-chloroethyl)-benzene in the above fraction. On refractionating Fraction II, 1-methyl-4-(α-ethoxyethyl)-benzene, b.p. 82-83° at 12 mm, was isolated. Yield 18 g (44%). A final purification of the product with sodium ethylate in ethyl alcohol did not change the boiling point.

n_D^{20} 1.4841; d_4^{20} 0.9122; MR_D 51.52; calculated 51.04.

0.1091 g substance: 0.3209 g CO_2; 0.0965 g H_2O. 0.1077 g substance: 0.1415 g AgI. Found %: C 80.27; H 9.90; OC_2H_5 25.2. $C_{11}H_{16}O$. Calculated %: C 80.44; H 9.82; OC_2H_5 27.4.

This ether is not listed in the literature. The residue after the distillation of the main product (3.5 g) crystallized in the flask. Crystals of di-p-tolyl, m.p. 121° were obtained after two recrystallizations from ethyl alcohol. The mixed melting point with synthetic di-n-tolyl was 121°, no depression in the melting point.

0.1155 g substance: 0.3902 g CO_2; 0.0803 g H_2O. Found %: C 92.20; H 7.78. $C_{14}H_{14}$. Calculated %: C 92.26; H 7.74.

12. Reaction of o-tolyl magnesium bromide with α-monochlorodiethyl ether. 43 g (0.25 mole) of o-bromotoluene, 7 g of maghesium, and 27.1 g (0.25 mole) of α-monochlorodiethyl ether were used for the reactions. The reaction conditions were those given earlier. Fraction I, to 77° (12 mm); Fraction II, 77-110° (12 mm) –19.5 g; residue –1.5 g. The amount of the chloride in Fraction II was determined by heating a weighed amount of this fraction with an alcoholic silver nitration solution.

0.1521 g substance: 0.0014 g AgCl. Found %: Cl 0.22. The amount of 1-methyl-2-(α-chloroethyl)-benzene was equal to 1.0%. After heating Fraction II with an ethyl alcohol solution of sodium ethylate, followed by a fractionation, 1-methyl-2-(α-ethoxyethyl)-benzene, b.p. 84-85° at 12 mm, was isolated.

n_D^{20} 1.4863; d_4^{20} 0.9263; MR_D 50.98; calculated 51.04.

0.1173 g substance: 0.3448 g CO_2; 0.1034 g H_2O. 0.1015 g substance: 0.1294 g AgI. Found %: C 80.22; H 9.86; OC_2H_5 24.5. $C_{11}H_{16}O$. Calculated %: C 80.44; H 9.82; OC_2H_5 27.4.

This ether is not listed in the chemical literature.

13. Reaction of duryl magnesium bromide with α-monochlorodiethyl ether. Starting materials: 35.5 g (1/6 mole) duryl bromide, 18 g (1/6 mole) ethyl bromide, 11 g of magnesium, and 36.2 g (1/3 mole) of α-monochlorodiethyl ether. Fraction I, to 112° (8 mm); Fraction II, 112-127° (8 mm) –16.0 g; residue –1.5 g.

As in the previous experiments, a weighed amount of Fraction II was warmed with alcoholic silver nitrate, to determine the amount of 1,2,4,5-tetramethyl-6-(α-chloroethyl)-benzene.

0.4005 g substance: 0.0128 g AgCl. Found %: Cl 0.79.

Thus the amount of the chloride in Fraction II is equal to 3.5%.

Fraction II was purified with sodium ethylate, followed by distillation and subsequent recrystallization from alcohol to give 1,2,4,5-tetramethyl-6-(α-ethoxyethyl)-benzene, m.p. 52-53° Yield 13.0 g (38%). This ether is not listed in the literature.

0.1139 g substance: 0.3393 g CO_2; 0.1101 g H_2O. 0.1081 g substance: 0.1161 g AgI. Found %: C 81.29; H 10.82; OC_2H_5 20.6. $C_{14}H_{22}O$. Calculated %: C 81.50; H 10.75; OC_2H_5 21.8.

SUMMARY

1. The unusual reaction between aryl magnesium halides and chloromethylalkyl ethers, in which orthodisubstituted aryl magnesium halides, in contrast to the orthomonosubstituted and unsubstituted, react with the above ethers to form the corresponding benzyl chlorides and not the normal products, the ethers, has been confirmed by new experimental material.

2. An experimentally upheld opinion as to the reason for this unusual reaction is given.

3. Monobromo- and monoiodomethyl ethers which are more active in comparison to monochloromethyl ether react normally, in contrast to the latter, with the orthodisubstituted aryl magnesium halides to form ethers, R–CH_2–O–CH_3. The benzyl bromides and iodides are formed only in almost insignificant amounts in these reactions.

4. α-Monochloroethylalkyl ethers, because of the greater activity of the chlorine atom as compared to the monochloroalkyl ethers, react with the aryl magnesium bromides to form normal reaction products, that is ethers of the type R–CH(CH_3)–O–R. The second reaction, namely that forming the chlorides, R–CHCl–CH_3, only takes place with reactions with orthodisubstituted aryl magnesium halides, and then only to a very insignificant extent.

5. In the process of this work, eleven substances, as yet unreported in the chemical literature, were synthesized and reported.

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THE PHENYLAMIDATION OF CARBOXYLIC ACIDS

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It was found earlier that amides were formed in good yields by the action of sulfonamides on the carboxylic acids [1], and that good yields of dialkyl amides were formed by the action of asymmetrical dialkyl sulfonamides on the carboxylic acids [2].

It was of considerable interest to see if carboxylic acids would be amidated with symmetrically substituted sulfonamides. The easily available sym. diphenylsulfonamide [3] and several aliphatic, aromatic, and heterocyclic acids were used as subjects for the experiments. It was found that the reaction proceeded very readily according to the following general reaction scheme:

$$RCOOH + C_6H_5NHSO_2NHC_6H_5 \longrightarrow RCONHC_6H_5 + C_6H_5NHSO_2OH.$$

Up to now one exception has been found, namely, the reaction of formic acid, which proceeds according to the following scheme:

$$HCOOH + 2C_6H_5NHSO_2NHC_6H_5 \longrightarrow HC(=NC_6H_5)(NHC_6H_5) + 2C_6H_5NHSO_2OH,$$

i.e., the formation of diphenylformamidine (with a yield of 86.7%) and not formanilide.

The yields of the phenylamides (acylanilides) are very good (see the Experimental section), in most cases over 90% of theory, and in some cases practically quantitative.

The direct phenylamidation of carboxylic acids can undoubtedly be used for the isolation and identification of the carboxylic acids because, as we know, the acylanilides are difficultly soluble in water and crystallize well. Only a few hundreds of a gram of the acid and a very short time are needed for the preparation of the necessary amount of the acylanilide for identification. The possibility that this reaction will be used industrially can not be excluded especially if good methods for the preparation of nuclear substituted diphenylsulfonamides can be found.

Name of acid	Yield of phenylamide % of theory	Recrystallization solvent for phenylamides	Melting points	
			Found	Literature values
Acetic	77.7	Water	114-115°	115°
Probionic	87.2	Alcohol + water	102-103	103-104
Isovaleric	79.1	Alcohol + water	103-105	109-111
Palmitic	89.7	Alcohol	83-84	87.5-90
Stearic	94.7	Alcohol	93-94	93.6
Phenylacetic	97.1	Alcohol + water	116-117	116-117
Benzoic	90.3	Alcohol	160-161	160-161
o-Chlorobenzoic	95.1	Alcohol	115-116	115
m-Nitrobenzoic	99.1	Alcohol	152-153	153-154
p-Nitrobenzoic	100.0	Alcohol	211-212	204
Nicotinic	80.8	Water (with $2H_2O$)	83-85	85 [5]

EXPERIMENTAL

A mixture of 0.01 mole of the carboxylic acid, 0.01 mole of symmetrical diphenylsulfonamide (2.24 g), and 5 ml of dry pyridine were heated in a 50-ml round-bottomed flask with a side arm for four hours on an oil bath heated to 115-120°. The pyridine was vacuum distilled to dryness on a boiling water bath, and the residue was worked up with 25 ml of 1N sodium hydroxide. The residue, in certain cases, had to be rubbed with a glass rod for some time in order to crystallize it. The phenylamide was then filtered, washed 4 times with (3 ml) water, and dried. In most cases almost colorless preparations were obtained, which melted only a few degrees below the pure substances. Completely pure acylanilides were obtained after one recrystallization.

The table contains the yield and melting point data of all of the phenylamides obtained by the direct phenylamidation of the carboxylic acids.

The yields of the acylanilides, noticeably soluble in water could probably be increased by extracting the aqueous filtrates and washings with ether, or some other suitable solvent, after removal of the acylanilides.

The diphenylformamidine was prepared and isolated in a manner similar to that used with the phenylamides, but for 0.01 mole or dry formic acid (0.46 g), 0.02 mole of diphenylsulfonamide (4.96 g) was used. The yield was 1.7 g, i.e., 86.7% of theory. The preparation melted at 136-137° after recrystallization from petroleum ether; according to the literature, diphenylformamidine melts at 135-136°, 138-139° [4].

SUMMARY

A method for the preparation of acylanilides by reacting the corresponding acids directly with diphenylsulfonamide was found.

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TRIMESINIC TRIANILIDE

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Curtius [1] obtained trimesinic trianilide in crystal form (from acetic acid), m.p. 118-120° (decomp.), by the prolonged heating of trimesinic triazide with aniline.

A trimesinic trianilide which darkened at 317° and melted at 320-321° when heated in a capillary was obtained by the action of diphenylsulfonamide [2] on trimesinic acid.

Usually the anilides of the lower melting carboxylic acids melt considerably higher than the free acids, and the anilides of the higher melting carboxylic acids melt either somewhat higher or lower than the free acids, not more than 40-50° [3]. The melting points of the amides and anilides of the higher melting carboxylic acids also do not differ by more than 40-50° [3]. The melting point of trimesinic acid is 350°, that of its amide 365° [3]; therefore it seemed very surprising that the anilide of trimesinic acid would melt at 118-120°. Apparently there is some error in the work of Curtius. In order to finally clear up this misunderstanding, the trimesinic trianilide, obtained by direct phenylamidation of trimesinic acid, was analyzed for its nitrogen, carbon, and hydrogen content. The quantities of nitrogen, carbon, and hydrogen corresponded to those for the trianilide. Therefore the melting point for trimesinic anilide should be corrected from 118-120° to 320-321°.

EXPERIMENTAL

A mixture of 0.05 mole of trimesinic acid (1.05 g), 0.015 mole of diphenylsulfonamide (3.72 g), and 7.5 ml of dry pyridine was heated for 3 hours on an oil bath heated to 115°. The pyridine was vacuum distilled, 25 ml of 1.0 N sodium hydroxide was added to the residue, and the pasty residue rubbed with a rod until it completely crystallized, which occurred after 4-5 minutes. The finely crystalline residue was filtered, carefully washed with water, and dried. The yield of trimesinic trianilide was 2.0 g, that is, 91% of theory. The substance was purified by recrystallizing it from a large amount of boiling alcohol (600 ml per g) or from boiling acetic acid (40 ml of acetic acid for 1 g). Yield, 0.80 g; coarse needles.

Trimesinic trianilide formed a finely crystalline colorless powder (from alcohol) or colorless shiny needles (from acetic acid). Trimesinic trianilide was difficultly soluble in all the common solvents. It darkened at 317° and melted at 320-321° (Berle-Coleman block, narrow range thermometer).

Found %: C 74.00; H 4.78; N 9.71. $C_{27}H_{21}O_3N_3$. Calculated %: C 74.42; H 4.86; N 9.65.

The authors are very grateful to N. A. Ilushin of the Organic Chemistry Institute of the Academy of Sciences of the USSR for the analysis of the compound.

SUMMARY

Trimesinic trianilide was produced by the direct phenylamidation of trimesinic acid, and was found to melt at 320-321°, and not at 118° as held by Curtius.

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* See Consultants Bureau translation, p. 1653.

HYDROXYMETHYLENE-(PHENYL) ACETIC ACID AND ITS DERIVATIVES

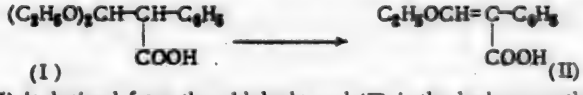
I. T. Strukov

In the present research, several derivatives of hydroxymethylene-(phenyl) acetic acid were studied in order to become acquainted with the physical and chemical properties of this series of organic compounds.

In Communication II [1], it was shown that hydroxymethylene-(phenyl) acetic acid could be prepared from diethoxymethyl-(phenyl) acetic acid by treating it with concentrated hydrochloric acid at 0°. In contrast to the method given in the literature [2], diethoxymethyl-(phenyl) acetic acid was prepared directly from formyl-(phenyl) acetic ester by heating it with an alcoholic solution of hydrochloric acid, followed by the saponification of the ester.

The unusual change in hydroxymethylene-(phenyl) acetic acid when dissolved in pyridine, its condensation with cysteine hydrochloride, as well as its unusually facile decarboxylation reaction, are of great theoretical interest.

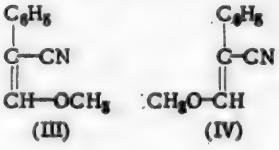
Hydroxymethylene-(phenyl) acetic acid, its amide, and nitrile exist, mainly, in the hydroxymethylene form, as shown by the color reaction with ferric chloride and by the absence of a reducing group when added to ammoniacal silver. However, the derivatives, are not only hydroxymethylene forms, but also the aldehydic forms of these compounds. For example, when diethoxymethyl-(phenyl) acetic acid (I) is reacted with thionyl chloride in chloroform, a molecule of ethanol is split off and ethoxymethylene-(phenyl) acetic acid (II) is formed.



(I) (II)

Substance (I) is derived from the aldehyde and (II) is the hydroxymethylene form.

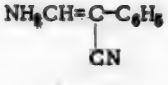
Methoxymethylene-(phenyl)-acetetonitrile is rather easily formed by the action of dimethyl sulfate on the sodium salt of hydroxymethylene-(phenyl)-acetonitrile [3]. Two forms of this compound are obtained, apparently the cis and trans forms. The cis form is a liquid (III), the trans form — a solid substance, m.p. 65-67° (IV).



(III) (IV)

Both forms are easily saponified by alcoholic alkalies and form hydroxymethylene-(phenyl)-acetonitrile. Benzyl cyanide is obtained at the same time.

Hydroxymethylene-(phenyl)-acetonitrile must be looked upon as an acid, and methoxymethylene-(phenyl)-acetonitrile as the ester of this acid. In fact, aminomethylene-(phenyl)-acetonitrile (V) is formed when the latter is treated with alcoholic ammonia.



(V)

Methoxymethylene-(phenyl)-acetonitrile does not give an iminoether. This is the latest differentiation of this compound from the nitriles. Although hydroxymethylene-(phenyl)-acetonitrile in not known in the aldehydic form, it is, however, apparently able to exist at certain times in the tautomeric aldehydic form, so that when it is heated with alcoholic hydrogen chloride, the acetal, diethoxymethoxy-(phenyl)-acetonitrile is formed, although not in good yield.

Ethyl aminomethylene-(phenyl)-acetate is obtained, instead of aminoethylene-(phenyl)-acetamide, by the action of alcoholic ammonia on ethyl methoxymethylene-(phenyl)-acetate (preparation [1]). Apparently in the above case, the methoxymethylene group behaves as an ester, being more labile than the usual ester group. Ethyl aminomethylene-(phenyl)-acetate has a peculiarity of its own: it forms diethyl iminobis-[methylene-(phenyl)-acetate] when treated with ethereal hydrogen chloride. Since similar transformations are unknown

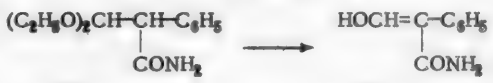
for usual amides, a very probable assumption can be made that the reaction occurs by means of the tautomeric form of aminomethylene-(phenyl)acetic ester (VI), the iminomethyl-(phenyl)-acetic ester (VII).

(VI) (VII)

Diethyl imino-(bis)-[methylene-(phenyl)-acetate] (VIII) was obtained in two forms, m.p. 152-154° (platelets) and m.p. 122-124° (long needles). There is the possibility of the change of the position of the double bonds in this compound

(VIII)

and there is no basis to consider them as really being cis and trans forms. In fact, if the possibility of the change of the position of the double bonds is excluded and considered to be a case of cis-trans isomerism, then, it is very hard to picture the formation of compound (VIII) from the aminomethylene-(phenyl) acetic ester (VI). Iminomethyl-(phenyl) acetic ester is an acid aldimine by virtue of the easy splitting of the imino group by the action of hydrogen chloride. Diethoxymethyl-(phenyl) acetic ester does not react with ammonia. For this reason diethoxymethyl-(phenyl) acetamide is obtained from diethoxymethyl-(phenyl) acetic acid. The anhydride of this acid is obtained by the action of thionyl chloride in chloroform in the presence of pyridine. Upon processing the anhydride in chloroform solution with aqueous ammonia, diethoxymethyl-(phenyl) acetamide (IX) is obtained in good yield, and on dissolving it in concentrated hydrochloric acid, the unstable hydrochloride of hydroxymethylene-(phenyl)-acetamide, and subsequently, the amide can be isolated.



(IX) (X)

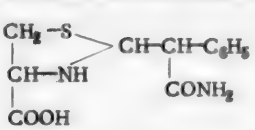
According to its reaction with ferric chloride solution and the absence of reducing power, compound (X) has the hydroxymethylene form. Therefore, in the process of splitting the acetal, the aldehyde group rapidly isomerizes to the hydroxymethylene group. By condensing compound (X) with cysteine hydrochloride, α-(4-carboxythiazolidyl-2)-phenylacetamide (XI) is formed, which shows the easy transformation of the hydroxymethylene-(phenyl)-acetamide into the aldehyde form. The many reaction possibilities of hydroxymethylene-(phenyl) acetamide, due to the reactivity of the hydrogens on the amide group and to the hydroxy group of the hydroxymethylene, is of great interest as a means for the preparation of a new class of organic compounds.

According to their properties, hydroxymethylene-(phenyl) acetic acid, its amide, and its nitrile closely resemble the organic acids and their derivatives, but differ in possessing new capabilities for chemical transformation.

EXPERIMENTAL

Ethoxymethylene-(phenyl) acetic acid. 2 g of freshly distilled thionyl chloride in 5 ml of absolute chloroform was added to 1 g of diethoxymethyl-(phenyl) acetic acid dissolved in 5 ml of absolute chloroform and the mixture left for 18 hours at 20-25°. The chloroform and excess of thionyl chloride were removed by blowing them out with air in a vacuum. The residual oil was dissolved in 10 ml of chloroform and the solution treated with 10 ml of a 5% sodium bicarbonate solution. The water layer was separated, treated with activated charcoal, filtered, and carefully acidified at 0° with dilute hydrochloric acid. A crystalline precipitate (prisms) separated. It was recrystallized from benzene (1:4) to which pentane was added to cloudiness. M.p. 134-135°.

Ethoxymethylene-(phenyl) acetic acid was very soluble in alcohol, ether, acetone, ethyl acetate, and benzene; it was insoluble in water, gasoline, and pentane. The acid decarboxylated at 160°



(XI)

4.921 mg substance: 7.56 ml 0.05 N $Na_2S_2O_3$. Found %: OC_2H_5 23.06. $C_{11}H_{12}O_3$. Calculated %: OC_2H_5 23.96.

Ethoxymethylene-(phenyl)-acetonitrile. 1.6 g of sodium, followed by 8 g of hydroxymethylene-(phenyl)-acetonitrile, was added to 70 ml of absolute ethyl alcohol, whereupon a voluminous light yellow precipitate of the sodium salt formed. 14 g of ethyl iodide was added to the flask and it was heated to reflux for 20 hours, protected by a calcium chloride tube. At the end of the reaction, the solution was filtered from the precipitated sodium salt of hydroxymethylene-(phenyl)-acetonitrile, the alcohol was distilled, and the residue was dissolved in 100 ml of ether. The ether solution was washed with water and dried with sodium sulfate. After removal of the ether, the residual oil was fractionated in vacuum, and a fraction with b.p. 146-148° at 5-6 mm was collected. Weight 2.0 g, a colorless oil.

15.291 mg substance: 8.65 ml 0.01 N H_2SO_4. 15.063 mg substance: 8.50 ml 0.01 N H_2SO_4. Found %: N 7.92, 7.90. $C_{11}H_{11}ON$. Calculated %: N 8.09.

A silver salt, rapidly darkening in the light, was formed by the action of a silver nitrate solution on an aqueous solution of the sodium salt of hydroxymethylene-(phenyl)-acetonitrile.

8 g of the silver salt of hydroxymethylene-(phenyl)-acetonitrile was stirred for 6 hours, at 15° with 10 g of ethyl iodide in 100 ml of water. The reaction mixture was extracted with ether, the ether solution was filtered and dried with sodium sulfate, and the residue distilled in vacuum. 2 g of a colorless oil, b.p. 145-148° at 5-6 mm, was obtained.

Methoxymethylene-(phenyl)-acetonitrile, its cis and trans forms. 74 g of a 42% potassium hydroxide solution was added slowly to 74 g of hydroxymethylene-(phenyl)-acetonitrile in 400 ml of water in a 1-liter round-bottomed flask equipped with a stirrer and immersed in an ice-water bath. . g of dimethyl sulfate was then added to the solution of the potassium salt of hydroxymethylene-(phenyl)-acetonitrile and the mixture stirred for 15 hours at 0°. A thick, lumpy mass separated. It was separated from the aqueous solution, dissolved in 400 ml of ether, and washed with a 40% potassium hydroxide solution. The ether solution was dried with sodium sulfate, the ether distilled, and the residue vacuum distilled. B.p. 142-145° at 3-4 mm.

Trans-methoxymethylene-(phenyl)-acetonitrile crystallized in the form of long platelets when the distillate was dissolved in 70 ml of warm ether and cooled to −10°. The substance was filtered, washed with cold ether, and recrystallized from ether. M.p. 65-67°. Readily soluble in alcohol, ether, benzene, and poorly in gasoline.

6.260 mg substance: 3.93 ml 0.01 N H_2SO_4. Found %: N 8.79. $C_{10}H_9ON$. Calculated %: N 8.8.

On concentrating the mother liquor to 35-40 ml and cooling it to −10°, a small amount more of crystals, m.p. 65-67°, was obtained. (In all cases the filtration was made on a funnel cooled with ice and salt). The ether was distilled from the second mother liquor and the residual oil cooled to −10°. The crystals which formed were filtered and recrystallized from a mixture of toluene and pentane. M.p. 65-67°.

A total of 26 g of trans-methoxymethylene-(phenyl)-acetonitrile was obtained.

The residual oil was refractionated in vacuum at 3 mm: Fraction I, 120-127°, −4 g; Fraction II, 127-128°, −19 g (oil); Fraction III, 128-130°, −0.5 g.

Fraction II contained cis-methoxymethylene-(phenyl)-acetonitrile. It did not crystallize even after long standing.

7.515 mg substance: 0.5714 mg N_2 (19.5°, 741.5 m). Found %: N 8.65. $C_{10}H_9ON$. Calculated %: N 8.8.

By the saponification of 1 g each of the cis- and trans-methoxymethylene-(phenyl)-acetonitrile with 10 ml of methanol and 3.3 ml of 2.0 N KOH for 48 hours at 15°, with subsequent processing, 0.4 and 0.45 g respectively of hydroxymethylene-(phenyl)-acetonitrile, m.p. 156-158°, were obtained. Thus both forms gave the identical substance.

Benzyl cyanide was detected in the liquors.

An attempt to prepare methoxymethylene-(phenyl)-acetiminoether hydrochloride from methoxymethylene-(phenyl)-acetonitrile by Pinner's method was unsuccessful. The unchanged starting material was recovered.

Diethoxymethyl-(phenyl)-acetonitrile. 23.2 g of hydroxymethylene-(phenyl)-acetonitrile was added to a solution of 1.7 g (preweighed) dry hydrogen chloride in 150 ml of absolute ethanol and the mixture heated to reflux, protected by a calcium chloride tube, for 13 hours on a water bath. Upon cooling, 2 g of sodium hydroxide in 10 ml of alcohol was added. The sodium chloride which separated was filtered off, the alcohol distilled, the residue worked up with 100 ml of benzene, and filtered from a precipitate. The benzene solution was washed with a potassium carbonate solution, dried with potassium carbonate, and the benzene distilled. The residual oil was fractionated in vacuum. A fraction with b.p. 145-150° at 8 mm, weight 8.2 g (23.5% of theory) was obtained. It was a slowly crystallizing, colorless oil, readily soluble in many organic solvents.

10.768 mg substance: 28.61 ml 0.5 N $Na_2S_2O_3$. Found %: OC_2H_5 39.88. $C_{13}H_{17}O_2N$. Calculated %: OC_2H_5 41.07.

Aminomethylene-(phenyl)-acetonitrile. A solution of 11 g of methoxymethylene-(phenyl)-acetonitrile in 50 ml of absolute ethyl alcohol was saturated with ammonia at 0°. After standing for two days at 15°, the ammonia and the alcohol were removed in vacuum. The crystals were filtered, washed with cold absolute alcohol, and recrystallized from benzene. They were six-sided, somewhat extended platelets, m.p. 133-134°. They were readily soluble in alcohol, ether, acetone, and warm benzene, and insoluble in water. The substance was unchanged when heated for 3 hours to 150°.

5.150 mg substance: 7.14 ml 0.01 N H_2SO_4. Found %: N 19.41. $C_9H_8N_2$. Calculated %: N 19.44.

Ethyl aminomethylene-(phenyl)-acetate. A solution of 10 g of ethyl methoxymethylene-(phenyl)-acetate in 50 ml of methyl alcohol was saturated with ammonia at 0°. After standing for 5 days at 10-15°, the ammonia and the alcohol were removed in vacuum. The residual oil was vacuum distilled and a fraction with b.p. 142-143° at 3 mm, weight 6 g, was collected. It was readily soluble in the common organic solvents.

10.990 mg substance: 5.81 ml 0.01 N H_2SO_4. 6.843 mg substance: 3.65 ml 0.01 N H_2SO_4. Found %: N 7.40, 7.47. $C_{11}H_{13}O_2N$. Calculated %: N 7.33.

Diethyl-imino-bis-[methylene-(phenyl)-acetate]. A crystalline residue was obtained when a stream of dry hydrogen chloride was passed into a solution of 2 g of ethyl aminomethylene-(phenyl)-acetate in 15 ml of ether for 2 hours, followed by the removal of the hydrogen chloride and the ether in vacuum. When it was worked up with toluene, the insoluble part was filtered and identified as common salt.

The toluene was vacuum distilled and the residue dissolved in 10 ml of methanol. The next day the crystals were filtered and recrystallized from methanol several times until the melting point remained constant at 152-154°. They were large colorless platelets.

6.453 mg substance: 0.242 ml N_2 (19.5°, 730 mm). 7.817 mg substance: 12.66 ml 0.02 N $Na_2S_2O_3$. Found %: N 4.20; OC_2H_5 24.31. $C_{22}H_{28}O_4N$. Calculated %: N 3.84; OC_2H_5 24.64.

When the first methanol solution was evaporated to 3-4 ml and cooled, crystals melting at 122-124° after two methanol recrystallizations were obtained. Long needles.

8.678 mg substance: 0.306 ml N_2 (21.5°, 738 mm). 7.761 mg substance: 12.66 ml 0.02 N $Na_2S_2O_3$. Found %: N 3.97; OC_2H_5 24.48. $C_{22}H_{28}O_4N$. Calculated %: N 3.84; OC_2H_5 24.64.

Diethoxymethyl-(phenyl)-acetamide. 1.65 ml of purified thionyl chloride and 15.2 ml of dry pyridine were added at 20° to a solution of 10 g of diethoxymethyl-(phenyl)-acetic acid in 250 ml of absolute chloroform. After 5 minutes, the solution was diluted with 250 ml of chloroform, washed 2 times with 150 ml of a saturated sodium bicarbonate solution, 2 times with 200 ml of 1.0 N hydrochloric acid and 200 ml of saturated salt solution. The chloroform solution was then shaken for 15 minutes with 50 ml of 25% aqueous ammonia, washed 2 times with 50 ml of water, 2 times with 200 ml of saturated salt solution, and dried with sodium sulfate The chloroform was vacuum distilled on the water bath. The residual crystals were twice recrystallized from toluene (1:5). Thin silky needles, m.p. 114-117°, weight 4 g.

7.053 mg substance: 0.381 ml N_2 (23.5°, 734 mm). Found %: N 6.01. $C_{13}H_{19}O_3N$. Calculated %: N 5.91.

Diethoxymethyl-(phenyl)-acetic acid was obtained on evaporating the aqueous ammonia solution to dryness, dissolving the residue in 50 ml of water, and acidifying carefully with 10% sulfuric acid. Weight 4.6 g, m.p. 118-119° after recrystallization from toluene (1:4). Diethoxymethyl-(phenyl)-acetamide could also be obtained by first preparing the mixed anhydride of diethoxymethyl-(phenyl)-acetic acid and benzoic or acetic anhydride and then heating it with aqueous ammonia. However, the yield was much lower.

Hydroxymethylene-(phenyl)-acetamide. A solution of 1 g of diethoxymethyl-(phenyl)-acetamide in 5 ml of concentrated hydrochloric acid was left at 0° for three hours. A white needlelike precipitate which separated, was filtered off, washed with concentrated hydrochloric acid, and dried in a vacuum desiccator over potassium hydroxide and sulfuric acid. Yield 0.7 g, m.p. 76-77° (decomp.). The substance was soluble in water and gave a violet coloration with ferric chloride solution.

The substance obtained was the hydrochloride of hydroxymethylene-(phenyl)-acetamide. All attempts to analyze the substance for chlorine gave unsatisfactory results, which indicated that the hydrochloride linkage with the amide group is unstable.

0.5 g of hydroxymethylene-(phenyl)-acetamide hydrochloride was mixed with 1 ml of water, 25 ml of ether, and 0.5 g of sodium bicarbonate. The substance dissolved in the ether. After drying with sodium sulfate and distilling the ether, the residue was recrystallized from a small amount of toluene; m.p. 99-101°; prisms. It was poorly soluble in cold water, readily in hot water, alcohol, toluene, and ether, and insoluble in petroleum ether. It gave a violet coloration with ferric chloride solution. It did not reduce silver. When it was dissolved in sodium hydroxide solution, it decomposed and a precipitate of phenylacetamide, m.p. 156° formed. It resembles hydroxymethylene-(phenyl)-acetic acid in its behavior toward bases.

4.868 mg substance: 0.363 ml N_2 (17.5°, 731 mm). Found %: N 8.43. $C_9H_9O_2N$. Calculated %: N 8.58.

α-(4-Carboxythiazolidyl-2)-phenylacetamide. 0.65 g of cysteine hydrochloride was added to a solution of 0.7 g of hydroxymethylene-(phenyl)-acetamide hydrochloride in 5 ml of dry pyridine. A solution formed on mixing, but soon became cloudy from a precipitate which was forming. After two days the crystals were filtered and washed with pyridine and dried in a vacuum desiccator over sulfuric acid; m.p. 149-150° (decomp.).

0.5 g of the substance was dissolved in 10 ml of water by the addition of several drops of 25% ammonia. The solution was filtered, cooled to 0°, and acidified with 10% sulfuric acid. Spherical clusters of needles separated slowly, were filtered off, washed with distilled water, and dried in a vacuum desiccator. The substance dissolved easily in water. It did not contain a free mercaptan group (reaction with ammonia and sodium nitroprusside). It decolorized 0.1 N iodine solution, which is characteristic for thiazolidine compounds; m.p. 172-173°.

8.118 mg substance: 0.706 ml N_2 (19°, 747 mm). 0.1530 g substance: loss on drying. 0.049 g. Found %: N 10.00; H_2O 3.2. $(C_{13}H_{14}O_3N_2S_2)H_2O$. Calculated %: N 10.19; H_2O 3.2.

SUMMARY

Derivatives of hydroxy-, alkoxy-, and aminomethylene-(phenyl)-acetic acid were prepared. Several peculiarities of this class of organic compounds were shown.

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* See Consultants Bureau translation, p. 1077.

XXI. THE QUANTITATIVE DETERMINATION OF SEVERAL NAPHTHALENE DISULFONIC ACIDS

A. A. Spryskov and B. I. Karavaev

The formation of four isomeric disulfonic acids upon sulfonation of naphthalene was already established in the 19th century. In 1934 Ufimtsev and Krivoshlikova [1] found the 1,7-isomer in the mixture of sulfonic acids, and, later, Chuksanova [2], the 1,3-isomer.

By the sulfonation of naphthalene to the disulfonic acids, a mixture consisting of 1,3-, 1,5-, 1,6-, 1,7-, 2,6-, and 2,7-isomers is obtained. However, the mixture obtained at lower temperatures apparently does not contain the 2,6-isomer, while that obtained at 140-160° does not contain the 1,5-isomer [3, 7]. A certain amount of mono- and trisulfonic acids is also produced during the sulfonation to the disulfonic acids.

The method for the determination of 2,6- and 2,7-disulfonic acids by means of the solubility of the mixture of the lead salts [4] cannot be used for the analysis of the sulfonation mixture. The method for the determination of the 1,5- and 2,6-isomers as barium and lead salts [3] has not been worked out. The methods for the determination of naphthalene 1,5-disulfonic acid by means of its m-xylidine salt and of the 1,6-acid as the β-naphthylamine salt [6] can be checked only in the absence of the 1,7-isomer, which is always present in the sulfonation mixture.

Korolev, Bilik, and Chuksanova [9] give two methods for the determination of 1,5-naphthalene disulfonic acid in a mixture with 1,6-naphthalene disulfonic acid and naphthalene trisulfonic acids, by saturation with benzidine and with sodium chloride. The methods were checked in the presence of 1,3-, 1,7-, and 2,7-isomers.

Ufimtsev and Krivoshlikova [1] give a method in which the sulfonic group is removed with oleum, followed by nitration and the reduction of the nitro compound. The relative amounts of the 1,6- and 1,7-disulfonic acids were determined in this manner. This type of method was used by Lantz [5], who nitrated the sulfonated mixture both in the cold and with heating. However, these methods of Lantz were tested in the absence of the 1,3- and the 1,7-isomers and were found to need many corrections, which had to be determined experimentally for each determination. The method for the determination of 1,5- and 1,6-isomers with the aid of amalgams [8] does not give satisfactory results.

The problem was to work out a method which could be used for the separate determination of the 1,5- and the 2,7-disulfonic acids in the presence of the 1,3-, 1,6-, and 1,7-isomers, and a method for the separate determination of the 2,6- and 2,7-disulfonic acids in the presence of the 1,3-, 1,6-, and 1,7-isomers, i.e., in sulfonation mixtures obtained at lower temperatures (to 120°) and at higher temperatures (from 140-165°).

As a basis for the method for the determination of the above isomers, their well known property of forming difficultly soluble salts with benzidine was used. The most difficultly soluble salts are the salts of the 2,6- and 1,5-acids, which are quantitatively precipitated under the conditions given below even at 60-65°. The benzidine salt of the 2,7-disulfonic acid dissolves somewhat more easily. It precipitates at 0°, although not quantitatively; and needs, for the determination of correct analytical results, the use of a constant correction.

EXPERIMENTAL

Analysis procedure. A sample of the pure sulfonic acids and sulfuric acid, or an approximately 1 g sample of the sulfonated mixture, was dissolved in 50 ml of water, the solution neutralized with 0.5 N caustic, and taken to a volume of 175 ml according to the mark on the beaker. 25 ml of a 10% barium chloride solution was added to the solution, which was heated to boiling, and then, after a few minutes, 50 ml of a benzidine hydrochloride solution (20 g of benzidine in 25 ml of hydrochloric acid, d 1.19, in 1 liter of water) was added to the hot solution, and it was once more heated to boiling. After cooling to 60-65°, the precipitated benzidine salts of the 1,5- or the 2,6-disulfonic acid were filtered, washed until a negative test for the chloride ion was given, transferred to a beaker, and titrated with 0.1 N alkali to phenolphthalein.

TABLE 1

Determination of the 1,5- and 2,7-isomers in artificially prepared mixtures

Used sulfonic acid in % of the total sulfonic acids							Found, in % of the total sulfonic acids		Error of the determination, in %	
1,5-	2,7-	1,6-	1,7-	1,3-	1,3,5-	α-	1,5-	2,7-	1,5-	2,7-
31.7	31.0	31.0	–	–	–	6.2	31.3	–	−0.4	–
56.5	10.3	16.5	–	–	–	16.6	55.2	–	−1.3	–
76.1	5.5	13.0	–	–	–	5.5	76.9	–	+0.8	–
40.2	52.0	7.8	–	–	–	–	40.2	52.6	0	+0.6
64.5	18.6	17.0	–	–	–	–	64.1	19.2	−0.4	+0.6
41.2	26.4	10.4	11.5	10.4	–	–	39.1	29.0	−2.1	+2.6
44.3	20.7	10.8	9.4	9.4	5.4	–	40.9	22.1	−3.4	+1.4
43.9	25.1	10.4	8.5	8.5	3.7	–	41.5	27.0	−2.4	+1.9
39.1	32.3	7.5	10.6	6.0	4.5	–	39.3	34.0	+0.3	+1.7

TABLE 2

Determination of the 2,6 and 2,7-disulfonic acids in artificially prepared mixtures. (Expt. 1,2,5,9 in the presence of sulfuric acid)

Used sulfonic acid in % of the total sulfonic acids							Found, in % of the total sulfonic acids		Error of the determination, in %	
2,6-	2,7-	1,6-	1,3-	1,7-	1,3,6-	β-	2,6-	2,7-	2,6-	2,7-
7.4	50.2	30.7	–	–	–	6.5	7.1	–	−0.3	–
16.0	47.3	22.9	–	–	–	13.8	15.4	–	−0.6	–
31.6	53.8	14.6	–	–	–	–	32.6	55.1	+1.0	+1.3
19.9	66.0	14.1	–	–	–	–	20.7	69.1	+0.8	+3.1
22.6	50.4	9.0	9.0	–	–	9.0	23.2	50.4	+0.6	0
9.8	67.3	9.1	6.9	–	6.9	–	9.2	66.5	−0.6	−0.8
21.9	40.8	8.3	8.3	10.3	–	10.3	21.5	42.1	−0.4	+1.3
31.6	29.5	8.0	12.7	10.1	8.0	–	31.4	27.1	−0.2	−2.4
29.2	33.0	10.5	10.5	10.5	6.2	–	30.3	29.7	+1.1	−3.3

The filtrate from the benzidine salt was stored on ice. The benzidine salt of the 2,7-disulfonic acid which precipitated on standing was filtered off, washed free of chloride (five ml washes), transferred to a beaker, and titrated with 0.1 N alkali. The amount of 2,7-disulfonic acid was calculated by the formula $\frac{1.44a + 2.26}{s}$ = % 2,7-disulfonic acid, where a is the amount of 0.1 N alkali used for the titration, s — the weight of the analysis mixture; 2.26 — a correction for the incomplete precipitation of the 2,7-acid (found experimentally to be the average of 10 precipitation experiments). The amounts of the 1,5- and the 2,6-isomers were found with this formula, but without the correction factor.

The precipitation of the benzidine hydrochlorides of the naphthalene disulfonic acids (250 ml vol.) showed that the 1,5-acid was precipitated to an extent of 99%, the 2,6-acid, −100%, and the 2,7-acid −96.5% of the amount taken.

The results of the tests of the method for the determination of the 1,5- and the 2,7-isomers, which are given in Table 1, show that for artificially prepared mixtures of the pure sulfonic acids, the error for the determination of the 1,5-acid amounts to 2-3%, for the 2,7-acid −2.5%, and sometimes even more. The use of two parallel determinations is considered necessary. In the latter case the error for the determination will be less than 2%.

It must be pointed out that when the amount of the 1,5-isomer in the mixture is less than 0.1 g (i.e. if the amount of 0.1 N alkali for the titration of the benzidine salt falls below 7 ml), very inaccurate results are obtained; in this case the amount of the sample of the sulfonated mixture must be increased.

The data in the table also show that this method was checked even when all of the mono-, di-, and trisulfonic acids which can be found in preparations at lower temperatures (100-120°) are present in the mixture.

The results in Table 2 of the tests of the method for the determination of the 2,6- and 2,7-isomers in artificially prepared mixtures of the pure sulfonic acids (0.43-0.68 g mixtures) show that the error for the determination of the 2,6-acid amounts to 1.2%, and for the 2,7 acid, 3.0%. With two parallel analyses the error will not exceed 2%.

Table 3 contains the results of the testing of the method on sulfonation mixtures produced by the direct

TABLE 3

Determination of the 1,5- and the 2,7-disulfonic acids in the sulfonated mixture obtained at 40-60° and with the addition of the 1,5- and 2,7-isomers

Sulfonic acids in the sulfonated mixture				Total (g)	Amount of pure acids added to the sulfonated mixture		Resulting amount of the sulfonic acids in %		Found after the addition, in %		Error, in % of the total sulfonic acids	
In % of the total sulfonic acids												
1,5-		2,7-	trisulfonic acids									
by the benzidine method	by the xylidine method				1,5- (g)	2,7- (g)	1,5-	2,7-	1,5-	2,7-	1,5-	2,7-
50.5	49.0	0	6.2	0.3887	0.1784	0.1036	55.9	15.4	56.4	—	0.5	—
58.6	56.9	0	1.2	0.3499	0.1796	0.2322	50.5	30.6	51.8	27.2	1.3	3.4
54.3	55.5	0	1.4	0.3360	0.1455	0.1546	51.6	24.3	55.0	24.3	3.4	0
54.3	55.5	0	1.4	0.1680	0.1604	0.1426	53.4	30.3	54.2	33.1	0.8	2.8
54.3	55.5	0	1.4	0.1680	0.1745	0.1472	54.3	30.1	55.7	31.0	0.4	0.9

TABLE 4

Determination of the 2,6- and 2,7-disulfonic acids in the sulfonated mixture at 162° and with the addition of pure 2,6- and 2,7-isomers

Sulfonic acids in the sulfonated mixture			Total (g)	Amount of pure acids added to the sulfonated mixture		Resulting amount of the sulfonic acids in %		Found after the addition, in %		Error, in % of the total sulfonic acids	
In % of the total sulfonic acids											
2,6-	2,7-	trisulfonic acids		2,6- (g)	2,7- (g)	2,6-	2,7-	2,6-	2,7-	2,6-	2,7-
18.3	52.5	0.4	0.6462	0.0856	0.0798	25.1	51.7	25.2	53.1	0.1	1.4
19.0	50.0	0.4	0.6462	0.1663	0.2503	27.2	54.2	27.2	56.4	0.2	2.2

sulfonation of pure naphthalene. The naphthalene was sulfonated with pure 25% oleum for 4 to 9 hours at 40-60°. The solution of the sulfonated mixture was made up to 500 ml and titrated with an 0.1 N alkali solution to determine the amount of the di- and trisulfonic acids. The amount of the 1,5-disulfonic acid was determined by the above method and by means of its xylidine salt [6]. The 2,7-disulfonic acid was not detected in the mixture. The pure 1,5- and 2,7-disulfonic acids were added to the solution and the mixture reanalyzed for amounts of the 1,5- and 2,7-disulfonic acids.

The analysis results given in Table 3 show that the error of the determination sometimes amounts to 3.4% of the total sulfonic acids. As the table shows, two parallel runs give as an average more satisfactory results. The xylidine and benzidine methods give results in close agreement.

The results of the tests of the method for sulfonated mixture obtained by the sulfonation of 0.216 moles of naphthalene with 1 mole of CP 100% sulfuric acid for 6 hours at 162° are given in Table 4. The mixture gave a clear colorless solution when poured into water. After determination of the di- and trisulfonic acids by titration with 0.1 N alkali, the amounts of the 2,6- and the 2,7-isomers were determined by the above method. Then pure 2,6- and 2,7-disulfonic acids were added to the solution, which was then reanalyzed for the amounts of the 2,6- and 2,7-isomers. The results show the error for the determination of the 2,6-isomer is extremely small, and for the 2,7-isomer, using two parallel analyses, less than 2%.

The method for the determination of the 1,5-isomer as the m-xylidine salt [6] was studied in the presence of the 1,3- and the 1,7-isomers. The results show that the xylidine method gives good results even in the presence of the 1,3- and 1,7-acids, if the amount of the 1,5-isomer in the analytical sample is not less than 0.1 g.

The above method cannot be used for technical sulfonated mixtures [9]. It is still thought that the precipitation of the arylamine salts is hindered, not by the naphthalene trisulfonic acids, at least when they are present in small amounts, but by other impurities in the technical mixtures. The above method can be used for sulfonated mixtures obtained from chemically pure naphthalene and pure sulfuric acid or oleum, and can serve as a method for the study of processes for the preparation and isomerization of the disulfonic acids under various conditions.

SUMMARY

. A very simple method for the determination of the amounts of the 2,6- and 2,7-naphthalene disulfonic acids in sulfonated mixtures obtained at high temperatures (140-165°) by means of their benzidine salts is given.

The method given earlier [9] for the determination of the 1,5-isomer by means of its benzidine salt was worked out and tested for the determination of the 1,5- and the 2,7-disulfonic acids in mixtures obtained at lower temperatures (to 120°).

The error for the determination of the 2,6-disulfonic acid does not exceed 1%, and the error for the determination of the 1,5- and 2,7-isomers with two parallel analyses does not exceed 2% of the total sulfonic acids.

The determination is made by a macro method and consumes little time.

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XXIII. PREPARATION OF THE ACID CHLORIDES AND OTHER DERIVATIVES OF THE NAPHTHOL DISULFONIC ACIDS

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The acid chlorides of the sulfonic acids are important not only for the identification and purification of the sulfonic acids, but also for the preparation of their derivatives. The existence of many known naphthol sulfonic acids makes their acid chlorides important for the achievement of the first and second aim. However, their preparation from the salts of the sulfonic acids by means of phosphorus chlorides is not possible; instead the phenolic hydroxyl is substituted by chlorine. The attempts of Claus and Mielcke [1] as well as Holt and Mason [7] in this direction cannot be considered successful, since the chlorides were not obtained in crystalline form.

The action of chlorosulfonic acid on 1- and 2-naphthols or naphthol monosulfonic acids leads to the formation of a mixture of disulfonyl chlorides and trisulfonyl chlorides. For example, a mixture was obtained from 1-naphthol and chlorosulfonic acid from which 1-naphthol-2,4-disulfonyl chloride [2], and 1-naphthol-2,4,7-trisulfonyl chloride were isolated. The action of chlorosulfonic acid on 2-naphthol produces a mixture from which 2-naphthol-1,6-disulfonyl chloride and 2-naphthol-1,5-disulfonyl chloride were isolated. By increasing the temperature, 2-naphthol-3,6,8-trisulfonyl chloride [2] may be obtained. 2-Naphthol-6-sulfonic acid and 2-naphthol-1-sulfonic acid give 2-naphthol-1,6-disulfonyl chloride when treated with chlorosulfonic acid [3]. 2-Naphthol-6,8-disulfonyl chloride is obtained from 2-naphthol-8-sulfonic acid. 2-Naphthol-1,5-, 2-naphthol-1,6- and 2-naphthol-1,7-disulfonyl chlorides may be obtained by the action of chlorosulfonic acid upon 2-naphthol-5-sulfonic acid, 2-naphthol-6-sulfonic acid, and 2-naphthol-7-sulfonic acids, respectively [4]. 1-Naphthol-2,4,7-trisulfonyl chloride can be obtained by the action of chlorosulfonic acid upon 1-naphthol-2-, 1-naphthol-4-, or 1-naphthol-7-monosulfonic acids [5], or on 1-naphthol-2,4- and 1-naphthol-2,7-disulfonic acids [6]. 1-Naphthol-4,6,8-trisulfonyl chloride is obtained from 1-naphthol-4,6- and 1-naphthol-6,8-disulfonic acids.

The claim of Steinkopf that 2-naphthol-3,6-disulfonyl chloride could be obtained by the action of chlorosulfonic acid upon Schaeffer's salt is erroneous. As has been shown by Pollak [3], Steinkopf obtained 2-naphthol-1,6-sulfonyl chloride, m.p. 111°.

The preparation of the naphthol sulfonyl chlorides by the action of chlorosulfonic acid on the salts of the corresponding sulfonic acids without the introduction of new sulfonic groups is not reported in the literature except for the preparation of sultone-sulfonyl chlorides from the salts of 1-naphthol-3,8- and 1-naphthol-4,8-disulfonic acids [6].

The mono amides of 1-naphthol-3,8- and 1-naphthol-4,8-disulfonic acids were obtained by the action of ammonia on the sultones. Almost nothing is given about the properties of these amides (for example their melting points) [9]. Holt and Mason [7] claim the preparation of 2-naphthol-3-sulfonamide; however, its analysis is not given, and its formation by the method given can be doubted. Finally, the preparation of 2-naphthol-6-sulfonamide from 2-hydroxy-6-chlorosulfoxy-1-naphthoic acids [8] must be mentioned.

The method for the preparation of naphthol disulfonyl chlorides by the action of chlorosulfonic acid upon the salts of the corresponding sulfonic acids was studied in the present work. Some amides and anilides of the naphthol disulfonic acids were also obtained.

EXPERIMENTAL

The work was conducted on two α-naphthol disulfonic acids (1,3,8- and 1,4,8-) and on two β-naphthol disulfonic acids (2,6,8- and 2,3,6-).

The derivatives of 1-naphthol-4,8-disulfonic acid. Technical sodium salt (Khalbaum) was used to prepare the acid chloride of 1-naphthol-4,8-disulfonic acid. It gave a salt, m.p. 187°, instead of 205° given in the

TABLE 1

Preparation of 1-naphthol-4,8-disulfonyl chloride by the reaction of the sodium salt of the acid with chlorosulfonic acid at 20° for 24 hours

Expt. No.	Materials taken			Yield of the chloride (in % of theoretical)	Melting point of the chloride	
	Salt of the naphthol-sulfonic acid, g	HSO_3Cl (in ml)	moles per 1 SO_3Na group		Crude	Once recrystallized
154	12	48	10	64.2	185°	197°
155	25	100	10	50.4	185	197
162	60	200	8	43.0	185	193
166	35	100	8	50.0	175	—

literature, with benzylisothiourea [12]. After one recrystallization, the melting point of the salt rose to 196° (without correction). Thus an impure salt was being used.

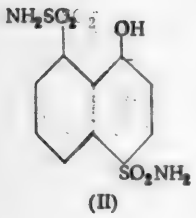
While the reaction vessel was cooled with cold water, the sodium salt was mixed with chlorosulfonic acid (redistilled at atmospheric pressure), and the mixture kept at room temperature (about 20°) without stirring for 24 hours. After the mixture was poured on ice, the chloride was filtered off, washed with ice water, and dried in a vacuum desiccator over sodium hydroxide sticks. The results of the experiments, listed in Table 1, show that the chloride was obtained in an average yield of slightly more than 50% of theory. The increase of the reaction time to 72 hours or the increase of the temperature to 60° did not improve the yield of the chloride.

The crystalline chloride obtained was not soluble in water, difficultly soluble in alcohol, and soluble in benzene. For recrystallization, the product was dissolved in benzene by warming, and after the addition of 1/4 volume of ether, cooled with ice and salt. A product, m.p. 197°, was obtained by one recrystallization in most cases. A second and third recrystallization did not raise the melting point. The amount of chlorine in the product indicated that it was the acid chloride sultone (I).

(I)

The product was analyzed by boiling with alkali and titrating by the Volhard method.

A considerable amount of the chloride remained unchanged after it was reacted with concentrated ammonia for 0.5 hours at 50-60°. After standing at room temperature for two days with the ammonia, the chloride dissolved completely. Apparently, the hydrolysis of the chloride, with the formation of the ammonium salt of the disulfonic acid, occurred. When dry ammonia was passed for one hour into a 3-5% solution of the chloride in benzene, a yellow precipitate formed, which consisted of a mixture of ammonium chloride and 1-naphthol-4,8-disulfonamide (II). The amide, unreported in the literature, was insoluble in benzene, ether, carbon disulfide, and dichloroethane.



(II)

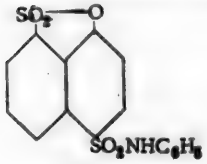
To separate the ammonium chloride from the amide, the mixture was twice dissolved in a small amount of water and filtered. The amide obtained did not contain any chloride ion or sulfonyl chloride and, even after boiling it with alkali, no chloride ion could be detected. The amide dissolved in water and alcohol, but could not be crystallized from them. The only way it could be purified was to dissolve it in alkali or in ammonia and precipitate it with acid to give a fine crystalline product. When it was treated with 10% alkali in the cold, saponification did not take place, and only at 60-70° did any energetic separation of ammonia occur. The product, which was dried in a desiccator, melted at 170-210°. After it was dried at 130°, the product lost 4.9% of its weight, but the melting point remained spread out. The amount of nitrogen in the product (7.95%, instead of the 9.26% calculated for $C_{10}H_{10}O_5N_2S_2$) also showed that it either contained water of crystallization or was not homogeneous.

The ammonia salt of the sulfonic acid, obtained by saponifying the chloride in dilute alkali, evaporating the solution to dryness, and neutralizing with ammonia, was recrystallized from water, forming platelets with m.p. 275-277°.

Upon heating the chloride of the sulfonic acid sultone with 4 moles of aniline in benzene solution for 30-40 minutes at temperatures not higher than 70°, followed by a 3 hour stay at 40°, aniline hydrochloride separated out. After filtering it off, the filtrate was evaporated in vacuum to half its volume. A crystalline precipitate, silver white scales, m.p. 145°, amounting to 30-40% of the chloride used, precipitated overnight. The melting point did not change after two recrystallizations from alcohol. The product did not dissolve in cold water, dissolved only slightly in hot water, and moderately in alcohol; it was very soluble in benzene, ether, and dichloroethane. The product appears to be the sultone sulfanilide (III).

0.7786 g substance: 21.79 ml 0.1 N HCl. Found %: N 3.87 (Kjeldahl). $C_{16}H_{11}O_3NS_2$. Calculated %: N 3.88.

If the benzene solution, after the preparation of the anilide, was filtered from the aniline hydrochloride, the benzene evaporated, and the residue dissolved in alkali, then a rupture of the sultone ring occurred and the sultone sulfanilide was changed to the sodium salt of 1-naphthol-4-sulfanilid-8-sulfonic acid, which was easily soluble in water. The aniline salt of 1-naphthol-4-sulfanilid-8-sulfonic acid (IV) separated when this solution, which contained aniline, was acidified with hydrochloric acid.

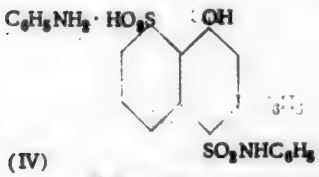


(III)

It was poorly soluble in cold water, but very soluble in hot water. It dissolved well in alcohol, and was not soluble in benzene and dichloroethane. The melting point, after more than one recrystallization from water, was 197°.

0.9643 g substance: 40.66 ml 0.1 N HCl. 0.7237 g substance: 30.53 ml 0.1 N HCl. Found %: N 5.91, 5.90. $C_{22}H_{16}O_6N_2S_2$. Calculated %: N 5.93.

The salt could be titrated with 0.1 N alkali in the presence of phenolphthalein. The results were better if an aliquot of the alkali was added to the salt and then back titrated with 0.1 N acid.



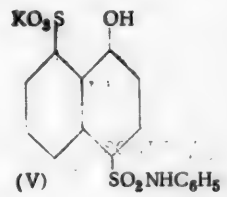
(IV)

0.1418 g substance: 2.98 ml 0.1 N NaOH. Found: M 475.1. $C_{22}H_{16}O_6N_2S_2$. Calculated: M 472.3.

If the sultone of 1-naphthol-4-sulfanilid-8-sulfonic acid, m.p. 145°, was dissolved in potassium hydroxide and acidified with hydrochloric acid in the absence of aniline, then the potassium salt of 1-naphthol-4-sulfanilid-8-sulfonic acid (V), separated. It was recrystallized from water and had a m.p. of 231-232°.

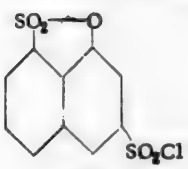
0.3234 g substance: 7.57 ml 0.1 N HCl. 0.1262 g substance: 0.0248 g K_2SO_4. Found %: N 3.32; K 8.82. $C_{16}H_{12}O_6NS_2K$. Calculated %: N 3.35; K 9.36.

The derivatives of 1-naphthol-3,8-disulfonic acid. The starting material was the technical sodium 1-naphthol-3,8-disulfonate of Kahlbaum, which was identified by its change to the sultone sulfonic acid upon heating it with sulfuric acid. The sultone sulfonic acid obtained melted at 240°. According to the literature, the melting point of the sultone sulfonic acid is 241° [11]. For the preparation of the acid chloride, the salt was mixed with redistilled chlorosulfonic acid and kept at room temperature for 24 hours. The mixture was then poured on ice, filtered off, washed, and dried in a vacuum desiccator. The results of the experiments, listed in Table 2, show that a yield of 86% was obtained from the once recrystallized salt. The crude chloride crystallized well from dichloroethane. After three recrystallizations, the melting point remained constant at 187-188°. The product was the sultone sulfonyl chloride (VI).



(V)

0.1828 g substance: 5.87 ml 0.1 N $AgNO_3$. Found %: Cl 11.39. $C_{16}H_9O_5S_2Cl$. Calculated %: Cl 11.64.



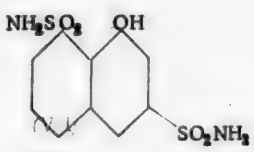
(VI)

Upon passing dry ammonia into a 3-5% solution of the chloride in dichloroethane, the amide precipitated almost quantitatively. It was insoluble in benzene, ether, carbon disulfide, and dichloroethane. It was moderately soluble in alcohol and water. The amide was purified by dissolving it in alkali and reprecipitating it with hydrochloric acid. The amide melted at 226-227° after drying at 120°.

0.5107 g substance: 30.31 ml 0.1 N HCl. Found %: N 8.88. $C_{16}H_{12}O_5N_2S_2$. Calculated %: N 9.26.

Therefore the product appears to have been 1-naphthol-3,8-disulfondiamide (VII).

The anilide of 1-naphthol-3,8-disulfonic acid was obtained by mixing a benzene solution of the sultone sulfonyl chloride (3.5 g in 100 ml) and aniline (4.05 g). When the solution was heated slightly, aniline hydrochloride separated. It was filtered after standing overnight, and the benzene distilled from the filtrate. The residue was recrystallized twice from alcohol over charcoal, and white crystals m.p. 213-213.5°, were obtained (VIII). The



(VII)

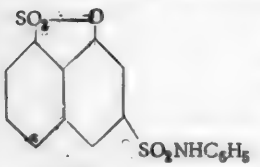
TABLE 2

Preparation of the chloride of 1-naphthol-3,8-disulfonic acid by the treatment of its sodium salt with chlorosulfonic acid at 15-20° for 24 hours

Expt. No.	Materials taken			Yield of the chloride (in % of the theoretical)	Melting point of the chloride		Notes
	Salt of the naphthol disulfonic acid (in g)	HSO_3Cl (ml)	HSO_3Cl moles per 1 SO_3Na group		Crude	Once recrystallized	
158	12	48	10.5	66.6	170-172°	–	
191	25	140	14.6	60.0	173-175	187°	
202	14.5	60	10.8	86.5	173	185	A once recrystallized salt was used

anilide obtained was soluble in alcohol, benzene, and ether, and poorly in water.

0.3292 g substance: 8.83 ml 0.1 N HCl. Found %: N 3.75. $C_{16}H_{11}O_5NS_2$. Calculated %: N 3.88.



(VIII)

The derivatives of 2-naphthol-6,8-disulfonic acid. The starting material was the technical sodium salt of 2-naphthol-6,8-disulfonic acid (Khalbaum). It gave a salt with m.p. 210-215° with benzylisothiourea, which, after recrystallization, melted at 220-221°.

For the preparation of the acid chloride, the sodium salt was mixed in the cold with redistilled chlorosulfonic acid, and the mixture heated for some time. Then it was poured on ice, washed by decantation, and filtered. The results of the experiments, listed in Table 3, show that the optimum conditions for the preparation of the chloride were to keep the reaction mixture for 2 hours at about 78° or somewhat lower.

It is apparent that with temperatures higher than the above, sulfonation took place, forming the trisulfonyl chloride.

The washing of the acid chloride on the funnel was very difficult because when it was squeezed it turned into a plastic tarlike mass, which only turned to a powder on drying in a desiccator or in the oven at 50-60°. Because of this, the product with the melting points listed in Table 3 still had not been completely freed of the mineral acid. For purification, the chloride was dissolved in benzene and precipitated with gasoline; a product with m.p. 157° was obtained. A recrystallization was needed to obtain the pure product, m.p. 161-162° [3].

When dry ammonia was passed into a benzene solution of the chloride, the amide precipitated. It was dissolved in alkali and reprecipitated with acid from the basic solution. The product did not contain chlorine and gave off ammonia when it was warmed with alkali.

The action of chlorosulfonic acid on 2-naphthol-3,6-disulfonic acid. Sodium 2-naphthol-3,6-disulfonate, purified by precipitation by alcohol from water, was used for the experiments. It gave a benzylisothiouronium salt, m.p. 233°. The same melting point is given in the literature for this salt [12].

The results of the reaction of the R-salt with chlorosulfonic acid, followed by pouring on ice, which are listed in Table 4, show that the chloride could not be obtained at lower temperatures. The chloride obtained at temperatures of 60-100° after one recrystallization from dichloroethane, had m.p. 170°, and after a series of recrystallizations, had m.p. 175°. When it was analyzed by titration of the base after saponification for chlorine content, it was shown that the trisulfonyl chloride had formed.

0.1255 g substance: 0.1190 g AgCl. 0.1048 g substance: 14.01 ml 0.1 N NaOH(after saponification). Found %: Cl 23.46; M 448.7. $C_{10}H_5O_7S_3Cl_3$. Calculated %: Cl 24.22; M 439.4.

Pollak et al [2] state that when 2-naphthol-3,6-disulfonic acid was treated with a ten-fold quantity of chlorosulfonic acid for 12 hours at room temperature, 2-naphthol-3,6,8-trisulfonyl chloride, m.p. 196°, was formed. The trichloride, m.p. 196°, was also isolated from the product of the reaction of 2-naphthol with a ten-fold excess of chlorosulfonic acid at 130-140° for 2.5 hours. The same chloride was obtained from 2-naphthol-1,5- and 2-naphthol-1,6-disulfonic acids, and 2-naphthol-3,6,8-trisulfonic acid at 130°.

TABLE 3

Preparation of the chloride of 2-naphthol-6,8-disulfonic acid by treating its sodium salt with chlorosulfonic acid

Expt. No.	Material used		Reaction temperature	Duration (in hours)	Chloride obtained	
	Salt of the naphthol disulfonic acid (in g)	HSO_3Cl (in ml)			Melting point	Yield (in % of theoretical)
229	4	16	16°	19	–	Low
239	4	16	40	6	133°	38.3
231	4	13	45-55	6	139	51.5
230	4	16	45-55	6	146-147	58.0
238	4	16	78	2	146	57.5
254	20	100	78	2	144-145	73.0
242	4	16	100	2	100-105	75.1

The acid chloride obtained is apparently 2-naphthol-1,3,6-trisulfonyl chloride, as was shown by the following. 2-naphthol-1,6-disulfonyl chloride, m.p. 111° [3], was obtained from 2-naphthol-6-sulfonic acid. When 2.2 g of this was heated with 9 ml of chlorosulfonic acid for 2 hours to 100°, a product with m.p. 153° was obtained. After recrystallization from dichloroethane and carbon disulfide, a product with a constant m.p. of 176.5° was obtained. A mixed melting point determination with the products obtained in Experiments 251, 243, and 244 gave no depression.

TABLE 4

The action of chlorosulfonic acid on sodium 2-naphthol-3,6-disulfonate

Expt. No.	Materials taken		Reaction temperature	Duration (in hours)	Chloride		
	R-Salt (g)	HSO_3Cl (ml)			Yield (in % of theoretical)	Melting point	
						Crude product	Recrystallized product
263	2.2	14	Room	18	No precipitate on ice		
262	2	20	Room	60	Precipitate melted in the air		
240	4	16	40°	6	Very little precipitate		
248	4	16	61	2	43	75-96°	–
251	4	16	61	6	45.2	130-135	169-171°
244	7	28	65-70	2	34	~ 138	175
241	4	16	78	2	43.8	~ 138	166-168
243	4	16	100	2	57.5	144-148	171

SUMMARY

1. The methods for the preparation of the sultones of 1-naphthol-3-sulfonylchloride-8 sulfonic acid, and 1-naphthol-4-sulfonyl-chloride-8-sulfonic acid, and 2-naphthol-2,6-disulfonyl chloride by means of the action of chlorosulfonic acid on the sodium salts of the corresponding naphthol sulfonic acids were studied.

2. The diamides of 1-naphthol-3,8-disulfonic acid, 1-naphthol-4,8-disulfonic acid, and 2-naphthol-6,8-disulfonic acid have been obtained for the first time.

3. The sultones of 1-naphthol-3-sulfonyl chloride-8-sulfonic acid and 1-naphthol-4-sulfonylchloride-8-sulfonic acid as well as the aniline and potassium salts of 1-naphthol-4-sulfanilid-8- sulfonic acid have been obtained for the first time.

4. 2-Naphthol-1,3,6-trisulfonyl chloride was obtained by the action of chlorosulfonic acid on 2-naphthol-3,6-disulfonic acid at 60-100°.

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RESEARCHES ON AMINO ACIDS

I. THE SYNTHESIS OF β-ALANINE

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The ability of acrylonitrile to add amines, amides, acids and other compounds to its double bond has been used for the synthesis of a whole series of valuable products [1]. β-Alanine is among these. There are several methods for preparing β-alanine from acrylonitrile. When acrylonitrile is heated with a concentrated aqueous ammonia solution, aminopropionitrile is obtained [2]. This gives β-alanine on hydrolysis. The method of preparing β-alanine from acrylonitrile by condensation with phthalamide, followed by saponification of the resulting phthalamidopropionitrile is interesting [3]. Because of the work of V. M. Rodionov and N. G. Yartseva, who employed an easily prepared catalyst for the condensation reaction of acrylonitrile and phthalamide, this method of preparing β-alanine became more feasible [4]. These authors also give an original method for separating β-alanine from its hydrochloride [5].

Among many methods unsatisfactory for various reasons [6], there is a method for preparing β-alanine from β-iodopropionic acid [7]. Certainly β-iodopropionic acid cannot be a convenient raw material for β-alanine, but the possibility of using β-halopropionic acid for the preparation of β-alanine was investigated in the present work.

In the place of iodopropionic acid, β-chloropropionic acid obtained in good yield by heating acrylonitrile and hydrochloric acid, was used.

$$CH_2{=}CH{-}CN \xrightarrow{HCl} \underset{\displaystyle Cl}{\overset{|}{CH_2}}{-}CH_2{-}COOH \xrightarrow{NH_3} \underset{\displaystyle NH_2}{\overset{|}{CH_2}}{-}CH_2{-}COOH$$

When β-chloropropionic acid is reacted with aqueous ammonia, the halogen atom is replaced by an amino group and β-amino propionic acid (β-alanine) is formed. After distillation of the ammonia solution, it separates in a mixture with iminodipropionic acid. β-Alanine is obtained in 50% yield from this mixture. When iminodipropionic acid is fused with phthalic anhydride, β-phthaloylaminopropionic acid, which can be used in the synthesis of pantothenic acid [4], is formed. By saponifying β-phthaloylaminopropionic acid, about 6% more of the theoretical amount of β-aminopropionic acid can be obtained.

EXPERIMENTAL

β-Chloropropionic acid was obtained according to the method in the patent literature [8], by heating acrylonitrile with hydrochloric acid, with yields of 82-85% of theory.

β-Alanine. 200 g (92%) of β-chloropropionic acid was dissolved in 4 liters of 22% ammonia solution and allowed to stand for 10-12 days. At the end of this period, 10 g of charcoal was added to the solution, which was filtered and evaporated to dryness in vacuum. 0.5 liter of conc. hydrochloric acid was added to the residue, and the mixture was boiled for 0.5 hours. The hydrochloric acid solution was evaporated in vacuum, and after removal of the hydrochloric acid, water was added twice to the residue and evaporated to dryness. The residue was freed of the last traces of moisture in a vacuum desiccator over phosphorus pentoxide. This dried residue was extracted with boiling 96% alcohol (500 ml) cooled, and filtered. The filtered salt was heated with 350 ml of 96% alcohol, filtered, and the filtrate combined with the first alcohol extract. 103 g of diethylamine was then slowly added until a pH of 7.6 was obtained. Small white crystals of β-alanine separated. On the following day, the crystals were filtered, washed three times with alcohol (50 ml) and dried. 71 g of β-alanine, m.p. 189-195°, was obtained. The alcoholic mother liquor and washings were evaporated to a volume of 200 ml and the semi-solid residue pressed carefully on the funnel in order to remove the bulk of the diethylamino hydrochloride. The filtrate was evaporated to dryness in vacuum and treated with 1.2 liters of cold chloroform, which dissolved everything except 34 g of a yellowish oil. This oil was once more triturated with a small amount of chloroform and the chloroform added to the main solution. The oil was allowed to stand and it crystallized completely (residual

β-alanine). 36% sodium hydroxide was added to the residue from the removal of the chloroform in vacuum and the diethylamine distilled.*

The basic solution freed from the diethylamine, was evaporated and the residue boiled with concentrated hydrochloric acid. After removal of the hydrochloric acid and the twice-added water in vacuum, the residue was extracted with alcohol. 4.5 g of β-alanine was isolated from the alcoholic extracts with diethylamine. The mother liquor, after the removal of the 4.5 g of β-alanine, was processed in the same way as the mother liquor after the removal of the first batch of β-alanine, and 3 g more was obtained. A total of 78.5 g of technical β-alanine was obtained.

For purification it was dissolved in the minimum amount of water and precipitated with eight volumes (in respect to the water) of alcohol. It was filtered, washed, and dried. More β-alanine was obtained after the evaporation of the alcohol-water solution, and the residue reprecipitated once more from water with alcohol. A total of 76.5 g, 50.6% of the theoretical amount, of β-alanine, was obtained; m.p. 195-197°.

Found %: C 40.24; H 8.10; N 15.70. $C_3H_7O_2N$. Calculated %: C 40.45; H 7.86; N 15.73.

Derivatives of iminopropionic acid were obtained from the 34 g of the oily product.

Diethyl iminodipropionate. A stream of dry hydrogen chloride was passed for 4 hours in the cold into a suspension of 22.4 g of the oil and 80 ml abs. alcohol. The oil slowly dissolved and the reaction mixture was boiled for 4 hours. The solution was evaporated in vacuum and the residue dissolved in 50 ml of water. Ether was added to the solution and it was carefully mixed with 30% sodium hydroxide until it was strongly alkaline. The ether was separated and the basic solution extracted several times with ether. The combined ether extracts were dried with fused sodium sulfate, and the ether removed. The residue was fractionated in vacuum at 15 mm. The fraction, up to 145°, did not contain any amino derivatives. Diethyl iminodipropionate hydrochloride was obtained from the fraction, b.p. 145-147°. 3.65 g of the ester was dissolved in 3 ml of absolute alcohol and treated with alcoholic hydrogen chloride until acid on Congo. Diethyl iminodipropionate hydrochloride was precipitated from this solution with dry ether as large colorless plates. After recrystallization from ethyl acetate, diethyl iminodipropionate hydrochloride melted at 78-79°.

Found %: N 5.77; Cl 13.80. $C_{10}H_{20}O_4NCl$. Calculated %: N 5.52; Cl 13.99.

β-Phthaloylaminopropionic acid. 11.4 g of the oil and 10.5 g of the phthalic anhydride was heated in a flask to 180-202° for 30 minutes. Acrylic acid and water distilled during the reaction. On cooling, the contents of the flask were dissolved in 60 ml of methanol and cooled. The precipitated crystals were filtered off and recrystallized once more from 60% methanol. The β-phthaloylaminopropionic acid obtained melted at 150-151°.

Found %: C 60.56; H 3.94; N 6.47. $C_{11}H_9O_4N$. Calculated %: C 60.27; H 4.11; N 6.39.

SUMMARY

1. β-Alanine was obtained in 50-56% yield by the reaction of β-chloropropionic acid with aqueous ammonia.

2. β-Alanine can be obtained from the hydrochloride by means of diethylamine.

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* The distilled diethylamine and the diethylamine obtained earlier from the hydrochloride were dried with caustic and distilled. A 60% recovery of the diethylamine was obtained.

SPECTROPHOTOMETRY OF BIURET COORDINATION COMPOUNDS AS A METHOD OF INVESTIGATION OF PROTEINS AND PEPTIDES

XIV. INFLUENCE OF THE AMINO ACID COMPOSITION OF THE PEPTIDES ON THE CHARACTER OF LIGHT ABSORPTION BY BIURET COORDINATION COMPOUNDS

M. I. Plekhan

The previous studies of the copper biuret coordination compounds of proteins [1-5] led to the conclusion that the properties of these complexes greatly resemble those of the coordination compounds of the tripeptides (diglycylglycine) and differ greatly from the coordination compounds of long-chain peptides. There was, however, a slight shift in the absorption maximum (10-15 mμ) of the protein coordination compounds toward the shorter wavelengths, suggesting the presence of some "red" complexes as impurities. This phenomenon can indicate the presence of a small amount (5-10%) of tetrapeptide in the protein molecule, along with the main mass of the tripeptides. Another explanation, however, is more probable. The tripeptide chains of the protein molecules, containing more complex amino acids than the simple tripeptide diglycylglycine, form coordination compounds with absorption maxima shifted toward the shorter wavelengths. This hypothesis could only be verified experimentally. It was necessary to explain the influence of the amino acid content of peptides on the biuret reaction. There is almost no data in the literature on this question.

The study of the biuret reaction of the polypeptides can be very complex because a large amount of peptides can be formulated by the permutation of the known amino acids. It was considered hardly expedient to run this volume of experiments, because of the concurrent great amount of experimental difficultly connected with the preparation of this great number of peptides and the improbability of its achievement.

TABLE 1

Amount of copper in the mixed amino acid tripeptide biuret complexes

Expt. No.	Tripeptide	Amount of copper per mole of peptide	
		(in g)	(in moles)
1	Glycylglycylglycine	61.6	0.97:1
2	Alanylglycylglycine	57.82	0.90:1
3	Leucylglycyltryptophan	65.8	1.03:1
4	Leucylglycylasparagine	52.9	0.83:1
5	Glycylglycylthreonine	44.0	0.69:1

For the present the study was limited to model di- and tripeptides in which one amino acid was made to be the carrier of the property to be studied. In this way, it was easier to establish the effect of each amino acid on the character of the coordination compound formation. In particular, bearing in mind the absorption spectrum of the glycyl tripeptide, it was of interest to determine the particular absorption which occurred when one of the glycine groups was changed to another amino acid. The following di- and tripeptides were prepared and studied: 1) glycylglycylthreonine; 2) leucylglycylasparagine; 3) leucylglycyltryptophan; 4) alanylglycylglycine; 5) carbobenzoxydiglycylglycine; 6) glycylthreonine; 7) glycylasparagine; 8) glycyltryptophan; 9) leucylhistidine; 10) glycyltyrocine; 11) carbenzoxyglycylglycine.

1. Copper Biuret Coordination Compounds of the Tripeptides

Solutions of the biuret coordination compounds were prepared in the usual manner (see the Experimental section).

The iodometric determination of copper in the peptide coordination compounds gave the following results, listed in Table 1.

The characteristic ratio between the copper and the peptide is equal to 1:1 for the first four tripeptide coordination compounds. The amount of copper in the glycylglycylthreonine complex is considerably lower than in all of the other complexes studied.

Spectrophotometric measurement of the absorption of light by the tripeptide copper coordination compounds showed that the influence of the various amino acids on the character of the absorption by the complex was far from being the same. Table 2 and Figure 1 contain the results of these measurements.

Analysis of the data obtained indicates the following:

1) A change of one of the glycine residues in the glycyl tripeptide to an alanine exerts an insignificant effect on the coordination compound; the position of the absorption maximum remains at the same wavelength [575 mμ] as in diglycylglycine, but the intensity of the absorption increases somewhat.

2) The introduction of asparagine into the tripeptide sharply changes the character of the coordination compound formation, a "red" coordination compound being formed, whose absorption maximum is the wavelength 525 mμ. Compared to the glycyl tripeptide coordination compound, the absorption maximum of leucylglycylasparagine is shifted towards the lower wavelengths by 50 mμ.

TABLE 2

Optical Density of the tripeptide copper biuret complexes (1/150 molar solutions)

No.	Wavelength λ (in mμ)	Magnitude of the optical density ε					
		Diglycylglycine	Glycylglycylthreonine	Leucylglycylasparagine	Leucylglycyltryptophan	Ananylglycylglycine	Carbobenzoxydiglycylglycine
1	480	0.222	0.233	0.325	0.336	0.212	0.066
2	505	0.310	0.341	0.425	0.472	0.310	0.108
3	520	0.360	0.387	0.458	0.526	0.384	0.137
4	525	—	—	0.458	—	—	—
5	530	0.392	0.407	0.458	0.550	0.435	0.155
6	535	—	0.410	0.451	—	—	—
7	540	0.416	0.412	0.445	0.564	0.480	0.168
8	545	—	0.411	—	—	—	—
9	550	0.442	0.411	0.428	0.578	0.520	0.177
10	560	0.451	0.405	0.402	0.589	0.550	0.179
11	570	0.460	0.393	0.371	0.595	0.565	0.176
12	575	0.463	—	—	0.596	0.570	—
13	582	0.443	0.378	0.334	0.597	0.562	0.171
14	585	—	—	—	0.596	—	—
15	595	—	—	—	0.590	—	—
16	600	0.423	0.344	0.278	0.584	0.550	0.152
17	610	0.393	0.322	0.248	0.570	0.499	0.142
18	620	0.374	0.299	0.216	0.545	0.447	0.128
19	630	0.351	0.272	0.188	0.514	0.417	0.106
20	640	0.330	0.243	0.161	0.482	0.365	0.093
21	650	0.313	0.215	0.140	0.441	0.318	—
22	670	0.280	0.158	0.100	0.358	0.224	0.081
23	693	0.240	0.107	0.067	0.264	0.138	0.039
24	710	0.191	0.078	0.050	0.200	0.090	0.031
25	730	0.134	0.054	0.036	0.146	0.060	0.025

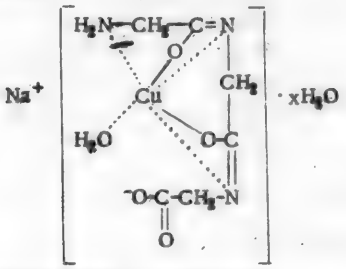
3) The introduction of threonine into the tripeptide molecule (glycylglycylthreonine) shifts the absorption maximum of the complex strongly toward the shorter wavelengths (540 mμ). The absorption is of mixed character lying between the absorption of the "red" and the "violet" coordination compounds. Compared to the glycyl tripeptide coordination compound, the maximum is shifted by 30 mμ.

4) The appearance of tryptophan in the tripeptide shifts the maximum slightly (by 7 mμ) toward the longer wavelengths (it lies at 582 mμ) and the intensity of the absorption is somewhat increased.

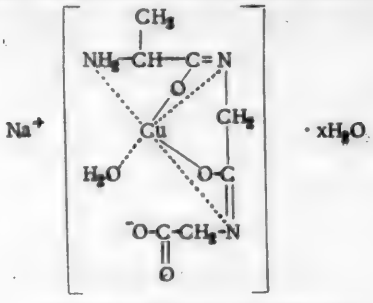
5) The change of one of the hydrogen atoms in the amino group of diglycylglycine to the carbobenzoxy group, shifts the absorption maximum of the complex by 15 mμ towards the shorter wavelengths [560 mμ].

Therefore, on the basis of these results an important conclusion can be drawn. The functional groups of the amino acids which make up the tripeptides enter into the formation of coordination compounds and exert specific influences on the character of the absorption. The entrance of alanine into the tripeptide does not shift the absorption maximum of the coordination compound, but only increases somewhat the intensity of the absorption. This indicates that the character of the bonds which determine the resulting absorption spectrum of an alanylglycylglycine coordination compound are the same as in the diglycylglycine complex. The plain CH_3 radical, as expected, does not form a bond with the copper atom, but the increase in the molecular volume leads to the increased

intensity of absorption. The specificity of the absorption of the biuret complexes, which, first of all is characterized by the position of the maximum and by the comparative intensity of absorption in various parts of the spectrum, must depend exclusively on the character of the coordination bonds between the copper atom and the groups capable of coordination compound formation. The following structures were considered possible for the coordination compound studied. The structure of the diglycylglycine coordination compound previously given is shown here for comparison.

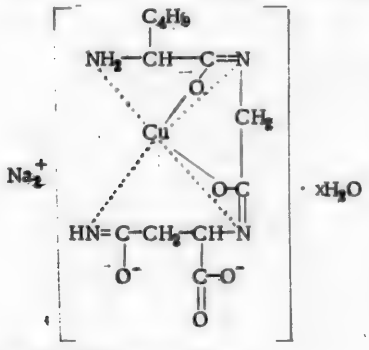


Diglycylglycine coordination compound



Alanylglycylglycine coordination compound

The fact that the appearance of a fourth nitrogen atom in the tripeptide leucylglycylasparagine (as compared to diglycylglycine) leads to the formation of a "red" coordination compound, instead of the "violet" characteristic of tripeptides, is considered to be of great importance.



Leucylglycyl-asparagine coordination compound

Of the three possible structural formulas for the leucylglycyltryptophan complex, the most probable is (III). If structure (I) was correct, then the absorption maximum would be shifted towards the shorter wavelengths and the color of the coordination compound would be red. According to structure (II), the nitrogen atom of the indole ring does not take any part in the coordination compound formation; according to this, the character of the absorption of the leucylglycyltryptophan coordination compound should be the same as for the diglycylglycine complex, differing only in the intensity of the absorption. Structure (II) cannot explain the 7 mμ shift toward the longer wavelength that is found for the leucylglycyltryptophan coordination compound.

Structure (III) provides for a saltlike link between the copper atom and the nitrogen atom of the indole ring. Of course supplementary experiments will be necessary to see if this linkage can be formed under the conditions of the biuret reaction.

Iodometric determination of copper in the glycylglycylthreonine coordination compound shows that there is more than one mole of the peptide for each atom of copper. It is possible that the iodometric method for the determination of copper gives lower figures in the presence of the tripeptide, glycylglycylthreonine. It is still difficult to propose a structure other than the one pictured above. Undoubtedly the cause of the very significant change in the character of the absorption spectrum when threonine is introduced into the tripeptide is due to the hydroxyl group taking part in the coordination compound formation.

2. Dipeptide copper biuret complexes

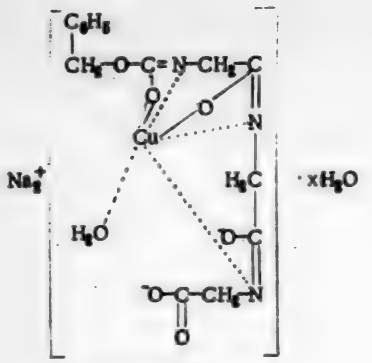
The results of the iodometric determination of the copper in dipeptide complexes are given in Table 3.

The amount of copper in all of the dipeptide complexes is somewhat low. Apparently the lack of reactivity for the formation of complexes is a general property of the dipeptides.

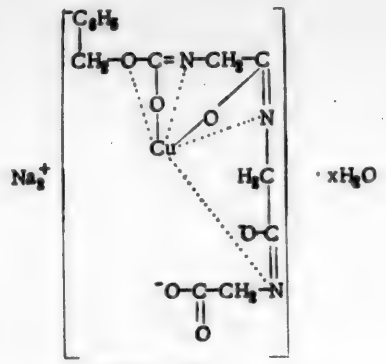
The spectrophotometric study of the dipeptide complexes led to the results given in Table 4 and Fig. 2.

The following conclusions were drawn from the results:

1. The absorption maximum of the glycylasparagine coordination compound lies at 532.2 mμ. The introduction of asparagine into the dipeptide sharply shifts the absorption maximum toward the shorter wavelengths (analogous results were obtained for the tripeptide leucylglycylasparagine).

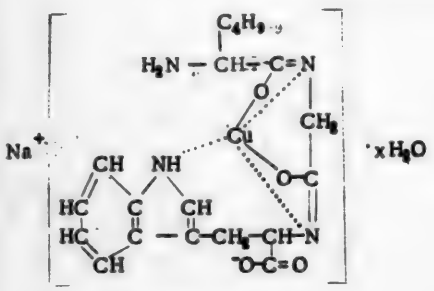


Schema (I)

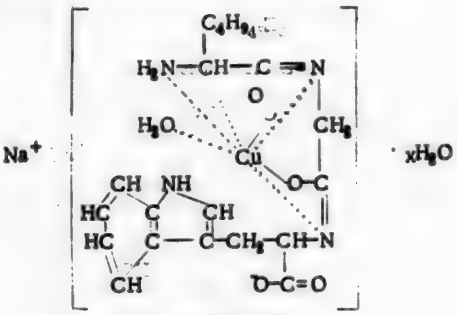


Schema (II)

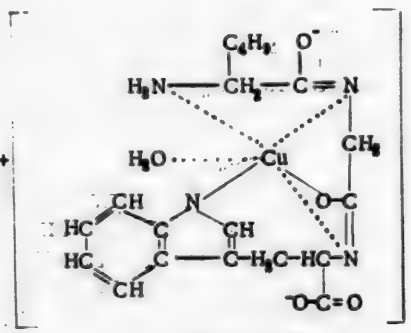
Carbobenzoxydiglycylglycine coordination compound.



Schema (I)

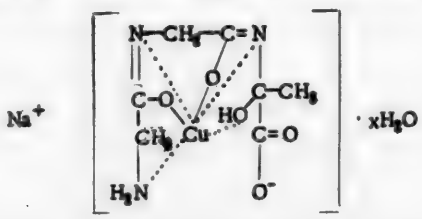


Schema (II)



Schema (III)

Leucylglycyltryptophan coordination compound



Glycylglycylthreonine coordination compound.

2. The absorption maximum of the glycylthreonine coordination compound lies at 645 mμ. The introduction of threonine into the dipeptide noticeably shifts the absorption maximum of the coordination compound toward the shorter wavelengths. (Analogous results were obtained for the tripeptide glycylglycylthreonine).

TABLE 3

Amount of copper in the dipeptide biuret coordination compounds

No.	Dipeptide	Amount of copper per mole of peptide	
		(in g)	(in moles)
1	Glycylthreonine	50.4	0.80:1
2	Glycylasparagine	53.6	0.84:1
3	Leucylhistidine	25.08	0.39:1
4	Glycyltyrosine	64.7	1.17:1
5	Glycylglycine	54.0	0.85:1

3. The absorption maximum of the glycyltyrosine coordination compound lies at 630 mμ. The introduction of tyrosine into the dipeptide shifts the absorption maximum of the coordination compound toward the shorter wavelengths.

4. The absorption maximum of the glycyltryptophan coordination compound lies at 630 mμ. The introduction of tryptophan shifts the absorption maximum of the coordination compound toward the shorter wavelengths. In this case a different phenomenon from that found for the tripeptide leucylglycyltryptophan is observed.

5. The absorption maximum of the carbobenzoxyglycylglycine coordination compound lies at 620 mμ. The replacement of one of the hydrogen atoms on the amino group leads to the shift of the absorption maximum of the coordination compound toward the shorter wavelengths.

Therefore an analogy is found in the behavior of the dipeptides and tripeptides, in the sense that the presence of different amino acids in the peptides leads to differences in the character of the absorption of the coordination compound. It is very interesting that the amino acid which causes the greatest shift in the absorption maximum of the tripeptide coordination compound has the greatest influence on the character of the absorption of the dipeptide coordination compound. For example, the introduction of asparagine into the tripeptide as well as the dipeptide causes an extremely sharp shift of the absorption maximum of the coordination compound. The absolute magnitude of the shift is not the same, as expected, as the structure of the dipeptide has its own peculiarities. Previously it had been considered that two molecules of the peptide and one copper atom form the coordination compound with glycylglycine. More correct determinations of copper and certain properties of this coordination compound have now led to the conclusion that the ratio is 1:1. Moreover, the dipeptide biuret coordination compound appears to be an incompletely formed coordination compound, and its activity of formation is considerably lower than for

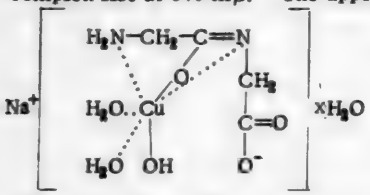
TABLE 4

Optical density of the dipeptide copper-biuret coordination compounds and their derivatives

No.	Wave length λ(in mμ)	Magnitude of the optical density, ε						
		Glycyl-glycine	Glycyl-threonine	Glycylas-paragine	Glycyl-tryptophan	Leucyl-histidine	Glycyl-tyrosine	Carbobenzoxy-glycylglycine
1	480	0.054	0.116	0.272	0.028	0.099	0.092	0.036
2	490	0.066	0.135	0.297	0.033	0.112	0.113	0.046
3	505	0.078	0.186	0.351	0.038	0.133	0.142	0.066
4	510	–	–	–	–	–	0.160	–
5	515	–	–	–	–	–	–	–
6	520	0.093	0.224	0.396	0.045	0.153	0.184	0.087
7	530	0.108	0.249	0.423	0.051	0.163	0.211	0.102
8	535	–	–	0.423	–	–	–	–
9	540	0.108	0.289	–	0.057	0.173	0.240	0.121
10	550	0.132	0.316	0.413	0.064	0.182	0.276	0.141
11	560	0.149	0.346	0.396	0.070	0.187	0.314	0.161
12	570	0.167	0.373	0.383	0.078	0.188	0.355	0.180
13	575	–	–	–	–	0.188	–	–
14	582	0.192	0.400	0.353	0.088	0.186	0.401	0.201
15	600	0.228	0.435	0.292	0.098	0.170	0.465	0.225
16	610	0.251	0.442	0.266	0.102	0.158	0.441	0.228
17	615	–	0.449	–	–	–	–	–
18	620	0.278	0.441	0.233	0.105	0.141	0.505	0.229
19	625	–	–	–	–	–	–	0.228
20	630	0.301	0.429	0.204	0.107	0.134	0.512	0.228
21	635	–	–	–	–	–	0.510	–
22	640	0.322	0.409	0.176	0.105	0.122	0.505	0.224
23	650	0.352	0.396	0.153	0.104	0.110	0.495	0.211
24	670	0.395	0.334	0.112	0.094	0.083	0.450	0.175
25	693	0.385	0.254	0.076	0.078	0.064	0.377	0.130
26	710	0.349	0.200	0.058	0.068	0.052	0.319	0.101
27	730	0.271	0.143	0.010	0.054	0.039	0.252	0.072

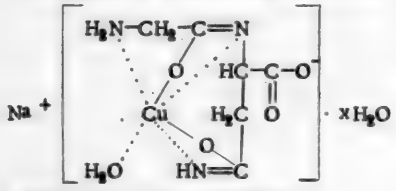
the tripeptide and somewhat higher than for the tetrapeptide. The blue color of the glycylglycine coordination compound and, in particular, the absorption of this coordination compound in the visible part of the spectrum, should be explained by the structure given below.

The incomplete nature of the glycylglycine coordination compound is explained only by the fact that the two coordinate valences are saturated by bonds with two molecules of water because of incomplete salt formation. One of the principal valences of copper remains bound with the hydroxyl. The absorption maximum of this complex lies at 670 mμ. The appearance of an amino acid containing a supplementary functional group in the dipeptide leads to a shift in the absorption maximum. It follows that one or the other of the bonds existing in the glycylglycine coordination compound is changed to bonds which are able to absorb at shorter wave lengths.

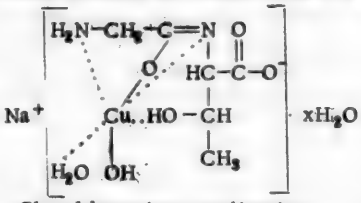


Glycylglycyl coordination compound

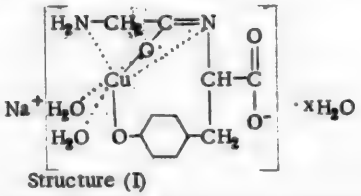
Of the two possible structures for the glycyltyrosine coordination compound the most probable appears to be (I), where a salt-forming bond exists between the copper atom and the phenolic hydroxyl.



Glycylasparagine coordination compound

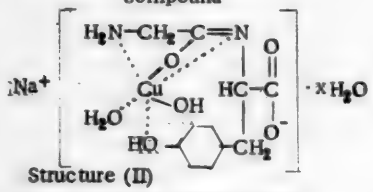


Glycylthreonine coordination compound



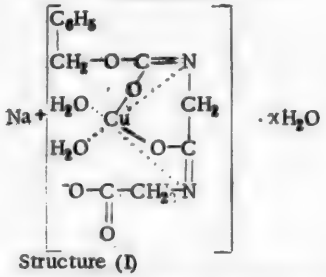
Structure (I)

Glycyltyrosine coordination compound

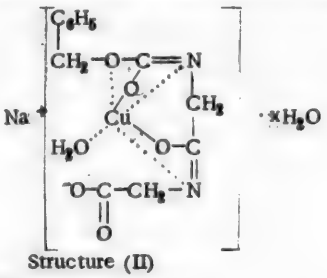


Structure (II)

Glycyl-tyrosine coordination compound

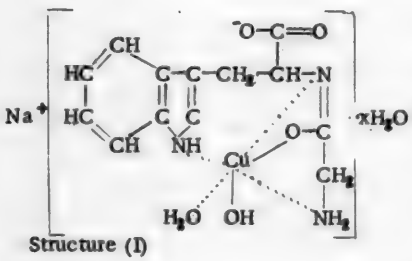


Structure (I)

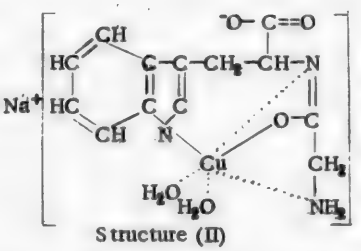


Structure (II)

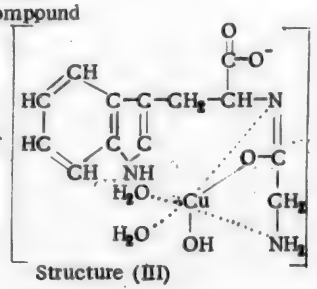
Carbobenzoxyglycylglycine coordination compound



Structure (I)



Structure (II)



Structure (III)

Glycyltryptophan coordination compound

Of the three possible structures for the glycyltryptophan coordination compound the most probable appears to be Structure (II). Structure (I) is less probable because the shift of the maximum in this case would be much greater, the coordination compound would have belonged to the "violet" group. According to Structure (III), the indole ring does not take part in the coordination compound formation, which gives no explanation for the change in the character of the absorption.

Reviewing the results obtained, it can be stated that in all cases (with one exception), the change of glycine in the tripeptide diglycylglycine and the dipeptide glycylglycine to an amino acid with some sort of supplementary functional group leads to the shift of the absorption to the shorter wavelength region.

The tripeptide containing asparagine forms the "red" coordination compound that containing threonine, the "red violet".

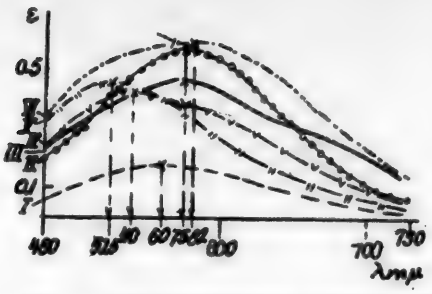


Fig. 1. Spectrophotometric curves of the tripeptide copperbiuret coordination compounds (1/150 molar solutions).

I) Carbobenzoxydiglycylglycine; II) alanylglycylglycine; III) diglycylglycine; IV) glycylglycylthreonine; V) leucylglycylasparagine; VI) leucyglycyltryptophan.

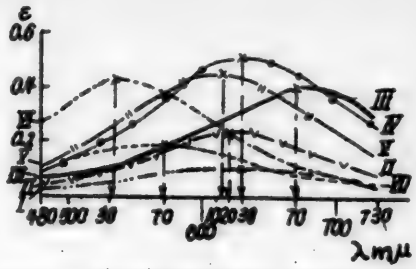


Fig. 2. Spectrophotometric curves of the dipeptide copper-biuret coordination compounds.

I) Glycyltryptophan; II) Carbobenzoxyglycylglycine; III) glycylglycine; IV) glycyltyrosine; V) glycylthreonine; VI) glycylasparagine; VII) leucylhistidine

The tripeptide chain in the protein molecule consists of many different amino acids, and for this reason the character of the absorption of the coordination compounds differs somewhat for different proteins. The shift of the absorption maximum toward the shorter wavelengths which is found with the protein coordination compounds as compared to the diglycylglycine coordination compounds can be best explained by the presence of various amino acids that form the peptide chain of the protein molecule.

EXPERIMENTAL

I. Synthesis of the Peptides.

1. Preparation of glycylthreonine. This compound was not reported in the literature. A method, based on that of Fischer and Rosner [6] for the synthesis of glycylserine, was used. Glycylthreonine was synthesized by reacting chloroacetyl chloride with the sodium salt of threonine, followed by the treatment of the chloroderivative with ammonia.

$$ClCH_2COCl + H_2NCHCOONa \longrightarrow ClCH_2CONHCHCOONa \longrightarrow H_2NCH_2CONHCHCOOH$$
$$\qquad\qquad\qquad\quad CHOH \qquad\qquad\qquad\quad CHOH \qquad\qquad\qquad\quad CHOH$$
$$\qquad\qquad\qquad\quad CH_3 \qquad\qquad\qquad\quad CH_3 \qquad\qquad\qquad\quad CH_3$$

2.1 ml of chloroacetyl chloride and 18 ml of 1N NaOH were added alternately in three portions over a 30 minute period to a solution of 1.5 g of threonine in 14.4 ml of 1N NaOH, well cooled with ice and salt. At the end of the addition, the stirring was continued for 30 minutes, after which time the solution was acidified with 14.4 ml of 1 N HCl. The clear colorless solution was left to stand for 1 hour. It was evaporated to dryness in vacuum. Toward the end, small portions of alcohol were added. The residue was treated three times with hot methyl acetate. The ester was distilled and an almost colorless oil remained. The oil was treated with 10 ml of 25 % aqueous ammonia for two days in the cold. The ammonia was vacuum distilled. The residue was dissolved in a small amount of water and precipitated with alcohol. The white precipitate was filtered, washed with alcohol and ether, and dried in a vacuum desiccator. It gave a violet-blue biuret reaction. The ninhydrin reaction was positive. A negative reaction for chlorine was given.

Found %: Total nitrogen 12.57. $C_6H_{12}O_4N_2 + 2H_2O$. Calculated %: N 12.39.

2. Preparation of glycylglycylthreonine. The compound was not reported in the literature.

$$ClCH_2COCl + H_2NCH_2CONHCHCOOH \longrightarrow ClCH_2CONHCH_2CONHCHCOOH \longrightarrow H_2NCH_2CONHCH_2CONHCHCOOH$$
$$\qquad\qquad\qquad\quad CHOH \qquad\qquad\qquad\qquad\quad CHOH \qquad\qquad\qquad\qquad\quad CHOH$$
$$\qquad\qquad\qquad\quad CH_3 \qquad\qquad\qquad\qquad\quad CH_3 \qquad\qquad\qquad\qquad\quad CH_3$$

0.6 ml of chloroacetyl chloride and 3.8 ml of 1 N NaOH were added alternately in 3 portions, over a 30 minute period, to a solution of 1 g of glycylthreonine in 6 ml of 1 N NaOH. The stirring was continued for 30 minutes or more. The solution was acidified with 7 ml of 1 N HCl. After an hour, it was evaporated to dryness. It was extracted with hot methyl acetate and the solution dried with Na_2SO_4 overnight, and the ether distilled;

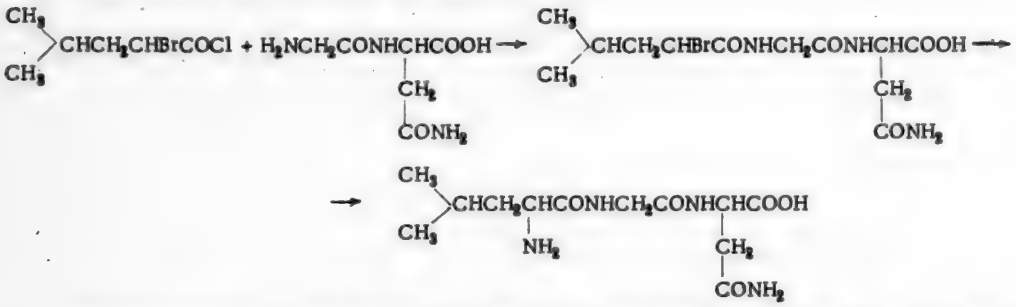
a light colorless oil remained. The oil was treated with 10 ml of 25% aqueous ammonia for two days in the cold. The ammonia was vacuum distilled, the residue dissolved in a small quantity of water, and precipitated with alcohol. A white precipitate formed overnight. The precipitate was filtered and washed with alcohol and ether. It was dried in a vacuum desiccator at 100°. The biuret reaction was positive. The Beilstein and $AgNO_3$ tests were negative. The ninhydrin reaction was positive.

Found %: Total nitrogen 18.12. $C_6H_{15}O_5N_3$. Calculated %: N 18.08.

3. Glycylasparagine, obtained by Fischer's method [7]. In the preparation of glycylasparagine, in the final stage it was found difficult to obtain it in the crystalline form. When glycylasparagine was precipitated from water with alcohol, it came out as an oil which was difficult to crystallize. A manifold treatment with absolute alcohol, however, resulted in the formation of fine white crystals.

4. Preparation of leucylglycylasparagine. This compound was not reported in the literature. Fischer's synthesis of leucylglycine-1-asparaginic acid was employed for the preparation.

The reaction went according to the equation:



0.8 ml of bromoisocaproyl chloride and 2.8 ml of 1 N NaOH were added alternately in three portions in one hour to a solution of 0.8 g of glycylasparagine in 4.5 ml of 1 N NaOH well cooled with ice and salt. It was acidified with 1.5 ml of 5 N HCl. A clear oil came out. The water was vacuum distilled. The residue, an oil, was dissolved in a small amount of ethyl alcohol and treated with 10 ml of a 25% aqueous solution of ammonia for two days. The ammonia was vacuum distilled. The residue was processed several times with boiling absolute alcohol. Finally, it was filtered rapidly, washed with absolute ether, and transferred to a vacuum desiccator, where it was dried over calcium chloride, and subsequently for 1 hour in the vacuum desiccator at 100°. Yield 27% of theory.

The substance gave a red-violet reaction. The ninhydrin reaction was positive.

Found %: Total nitrogen 17.43. $C_{12}H_{22}O_5N_4 + H_2O$. Calculated %: N 17.49.

5. Synthesis of glycyltryptophan and leucylglycyltryptophan was accomplished by the method of Abderhalden and Kempe [8].

6. Synthesis of glycyltyrosine and alanylglycylglycine was effected by Fischer's method [9].

II. The Spectrophotometry of the Biuret Coordination Compounds

Solutions of the biuret complexes were prepared in the following manner: A sample of the peptide calculated to a 1/150 molar concentration, was dissolved in 7 ml of water, 2 ml of NaOH, and 1 ml of 1/4 molar copper acetate. After one hour, the trace of copper hydroxide was filtered off. The solution was examined spectrophotometrically on a Beckman instrument.

The amount of copper in the biuret coordination compound solution was determined iodometrically.

SUMMARY

1. The change of one of the glycines in the tripeptide diglycylglycine to amino acid containing a supplementary functional group leads to the shift in the absorption maximum of the copper-biuret coordination compound toward the shorter wavelengths. The influence of the amino acid varies. An extremely large shift occurs with the appearance of asparagine in the tripeptide.

2. The change of one of the glycines in the dipeptide glycylglycine to amino acid with a supplementary functional group leads to a shift in the absorption maximum of the biuret coordination compound (to a varied degree) toward the shorter wavelengths. An extremely strong effect is felt with the appearance of asparagine in the dipeptide.

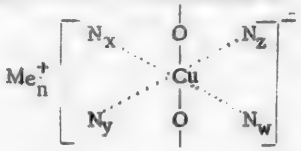
3. Oxygen containing groups (for example the hydroxy group of tyrosine and threonine) in the di- and tripeptides take part in coordination compound formation. The coordination bonds of the oxygen-containing groups absorb at longer wavelengths than the coordination bonds of nitrogen-containing groups.

4. The absorption of light of the biuret complex appears to be somewhat of an additive effect of the absorption of the separate bonds. The absorption of light by the coordinate bonds formed by the various groups – the coordination compound formers – appears to be somewhat characteristic for each bond. The position of the absorption maximum of the biuret complex depends on the coordination bonds; the intensity of absorption on the molecular weight.

5. This combined ability to absorb light is suggested as a basis for the classification of the biuret coordination compounds. The coordination compounds may so be separated into three main groups:

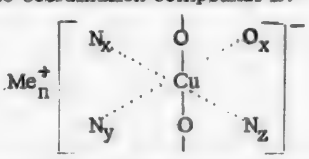
I. "Perfect" reds – formed with four nitrogen-containing groups; the absorption maximum of the coordination compound is at 515-535 mμ.

The general structure of these coordination compounds is:



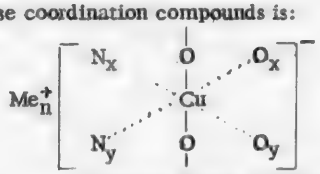
II. "Imperfect" violets – formed by three nitrogen-containing groups and one oxygen-containing group. The absorption maximum of the coordination compound is at 540-580 mμ.

The general structure of these coordination compounds is:



III. "Imperfect" blues – formed by two nitrogen-containing groups and two oxygen-containing groups. The absorption maximum of the coordination compounds is at 615-670 mμ.

The general structure of these coordination compounds is:



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*See Consultants Bureau translation, p. 2181.

**See Consultants Bureau translation, p. 341, 347, 635, 641.

SOME REACTIONS OF CYANOETHYLATION PRODUCTS OF DIHYDRIC PHENOLS WITH ACRYLIC ACID NITRILE

B. A. Arbuzov and Z. G. Isaeva

Cyanoethylation by means of acrylic acid nitrile acting upon compounds containing active hydrogen, in the presence of alkaline catalysts, has been widespread. A complete review of the literature of cyanoethylation has been given by Bruson [1].

Phenols react with acrylic acid nitrile in the presence of sodium, giving the corresponding cyanoethyl ethers [1]. As to dihydric phenols, there are patent facts that pyrocatechol and hydroquinone cyanoethylate in the presence of 1% sodium at 120-140°, giving mono- or di-cyanoethyl ethers, depending upon the amount of acrylic acid nitrile [2]. Resorcinol, according to the data of Langley and Adams [3], condenses with acrylic acid nitrile in the presence of hydrogen chloride and of zinc chloride, giving the lactone of β-(2,4-dihydroxyphenyl)-propionic acid. Cook and Reed [4] cyanoethylated pyrocatechol, resorcinol, and hydroquinone in the presence of sodium methylate, and obtained corresponding di-β-cyanoethoxybenzenes. Bachman and Levine found [5] that resorcinol in the presence of "Triton B" gives, 1,3-bis(β-cyanoethoxy)-benzene in 40% yield.

Knowledge of cyanoethylation of dihydric phenols is confined to these data.

The authors cyanoethylated pyrocatechol, resorcinol and hydroquinone in order to study certain transformation products of cyanoethylation. The yields and boiling points of the dicyano ethers obtained correspond to the data of Cook and Reed, excluding 1,4-di-β-cyanoethoxybenzene, for which the authors obtained a 70% yield, instead of 50% as indicated by Cook and Reed.

In the present article are cited data on saponification, alcoholation, and certain cyclization reactions of the obtained dinitriles.

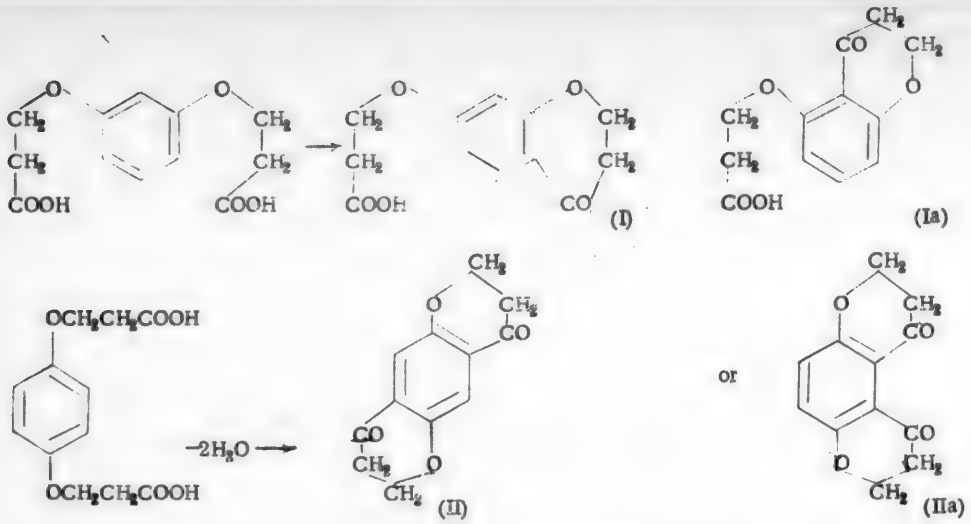
Saponfication of nitriles by 35% hydrochloric acid gave the corresponding dibasic acids. 1,2-Di-β-carboxyethoxybenzene had an m.p. of 155-157°, 1,3-di-β-carboxyethoxybenzene, m.p. 173-175°, and 1,4-di-β-carboxyethoxybenzene, m.p. 197-199°. 1,3-Di-β-cyanoethoxybenzene, by the action of alcohol in the presence of hydrogen chloride, was converted into the diethyl ester, b.p. 195-197° at 4.5 mm and m.p. 39-40°, which, upon saponification, gave the same acid with m.p. 173-175°. By the action of thionyl chloride on the obtained acids, corresponding full chloranhydrides were obtained. The chloranhydride of 1,3-di-β-carboxyethoxybenzene had an m.p. of 71-74°. In the case of 1,4-di-β-carboxyethoxybenzene, the full chloranhydride resulted, m.p. 91-93°.

The authors also conducted some cyclization experiments on the obtained free acids of 1,3- and 1,4-derivatives of benzene. Bachman and Levine [5] carried out cyclization of 1,3-di-β-cyanoethoxybenzene with 85% sulfuric acid, and obtained a product in 12.8% yield, m.p. 171-173°, to which they gave the structure 7-β-carboxyethoxychromanone [1]. The authors conducted cyclization reactions of 1,3-di-β-carboxyethoxybenzene by heating it with phosphoric anhydride, phosphoric acid being present. This gave a product with an m.p. identical to the product of Bachman and Levine, but in considerably greater yield (43.6%). The validity of its structure (Ia) was not studied.

The cyclization product contains one free carboxyl group, and upon reaction with semicarbazide hydrochloride gave a semicarbazone, m.p. 219-220°, which the authors were not able to obtain in an analytically-pure state.

Upon heating 1,3-di-β-carboxyethoxybenzene with phosphoric anhydride in phosphoric acid, a crystalline product was obtained, m.p. 229-230°, 23.2% yield, corresponding to the diketone.

The structure, in the sense of choice between (II) and (IIa), was not determined by the authors.



EXPERIMENTAL

Saponification of 1,2-di-β-carboxyethoxybenzene by hydrochloric acid. Taken for reaction were 1.4 g of 1,2-di-β-cyanoethoxybenzene, m.p. 118-120° and 20 ml of 35% hydrochloric acid. The mixture was heated on a water bath until the 1,2-di-β-cyanoethoxybenzene dissolved. Upon cooling of the reaction mixture, crystals separated, which were filtered off, washed with water and dried. Weight 0.53 g (32.6% yield) m.p. 155-157°. Recrystallization from alcohol did not change the m.p.

0.0926 g substance: 0.1700 g CO_2; 0.0518 g H_2O. 0.1044 g substance: 0.2016 g CO_2; 0.0564 g H_2O. Found %: C 52.72, 52.66; H 6.21. 6.00. $C_{12}H_{12}O_6$. Calculated %: C 56.69; H 5.51. $C_{12}H_{14}O_6 \cdot H_2O$. Calculated %: 52.94; H 5.88.

Saponification of 1,3-di-β-cyanoethoxybenzene by hydrochloric acid. Taken for reaction were 5 g of 1,3-di-β-cyanoethoxybenzene, m.p. 110-111°, and 25 ml of hydrochloric acid. The mixture was heated at 60-65° for 8.5 hours. The product was filtered, washed with water and dried, m.p. 172-175°. After a double recrystallization the product melted at 173-175°. Weight 3.9 g (yield 66.4%).

0.0980 g substance: 0.2028 g CO_2; 0.0514 g H_2O. Found %: C 56.49. H 5.82. $C_{12}H_{14}O_6$. Calculated %: C 56.69; H 5.51.

Alcoholysis of 1,3-di-β-cyanoethoxybenzene. 5 g of 1,3-di-β-cyanoethoxybenzene was dissolved in 150 ml of absolute ethanol. Dry hydrogen chloride was passed through the solution heated to boiling for 14 hours. The precipitated ammonium chloride sediment was filtered off. The filtrate was poured into water and extracted with ether. The ether extract was dried with calcium chloride. The ether was distilled off, and the residue distilled in vacuo. Obtained was 1.4 g of product, b.p. 195-197° at 4.5 mm, yield 19.7%. On standing, the product crystallized, m.p. 39-40°.

0.1206 g substance: 0.2727 g CO_2; 0.0786 g H_2O. Found %: C 61.67; H 7.24. $C_{16}H_{22}O_6$. Calculated %: C 61.90; H 7.15.

Saponification of the ethyl ether of 1,3-di-β-carboxyethoxybenzene. 0.3 g of the ether and 5 ml of 35% hydrochloric acid were heated on a water bath at 40-50° for 30 minutes. Upon cooling a precipitate settled out, which was filtered, washed with water and dried. After two recrystallizations from ethanol, 0.25 g of substance was obtained, m.p. 172-174°. The sample was mixed with 1,3-di-β-carboxyethoxybenzene, obtained by saponification of 1,3-di-β-cyanoethoxybenzene, and the mixture melted at 172-174°.

Reaction of thionyl chloride with 1,3-di-β-carboxyethoxybenzene. 3.5 g of 1,3-di-β-carboxyethoxybenzene and 15 ml of dry benzene in 16.2 g thionyl chloride were taken for reaction. The mixture was carefully heated upon a water bath until the 1,3-di-β-carboxyethoxybenzene dissolved. After distilling off the benzene and thionyl chloride in vacuo, there remained in the flask a pasty mass which partially crystallized. The chloranhydride was extracted with gasoline by warming. Crystals separated from the extract in very small quantity, which, after two recrystallizations from cyclohexane, melted at 71-74°.

0.0444 g substance: 0.0436 g HgCl. Found %: Cl 24.30. $C_{12}H_{12}O_4Cl_2$. Calculated %: Cl 24.39.

Cyclization of 1,3-di-β-carboxyethoxybenzene. Taken for reaction were 4.8 g of product, 50 g of phosphoric anhydride and 100 g of phosphoric acid (1.75). 6.6 times the theoretical weight of phosphoric anhydride necessary for splitting out two molecules of water from the dibasic acid was used. The mixture was heated 4 hours on a water bath. After cooling, the mixture was poured into cold water. The precipitate was filtered off, washed with water and recrystallized from alcohol. 1.9 g of substance, m.p. 169-171, was obtained. Yield of monoketone, 46.3%.

0.0994 g substance: 0.2224 g CO_2; 0.0754 g H_2O. Found %: C 61.02; H 5.20. $C_{12}H_{12}O_5$. (monoketone). Calculated %: C 61.01; H 5.12.

The product with an m.p. of 169-171 was titrated with NaOH solution (NaOH = 0.01928N): 0.0414 g of substance dissolved in 34 ml redistilled alcohol required 0.6 ml of the NaOH solution. Blank test – for 34 ml alcohol, 0.25 ml NaOH solution: given weight of substance required 0.85 ml NaOH solution.

Found: 0.006748 g NaOH. $C_{12}H_{12}O_5$. Calculated: 0.00701 g NaOH.

1,4-Di-β-cyancethoxybenzene saponification by hydrochloric acid. 5.2 g of the condensation product of hydroquinone with acrylic acid nitrile was saponified by 35% hydrochloric acid by heating on a water bath for 10 hours. After two recrystallizations from acetic acid 5.2 g of substance, m.p. 197-199°, was obtained, yield 85.2%.

0.0932 g substance: 0.1932 g CO_2: 0.0498 g H_2O. Found %: C 56.53; H 5.93. $C_{12}H_{14}O_6$. Calculated %: C 56.69; H 5.51.

Reaction of thionyl chloride with 1,4-di-β-carboxyethoxybenzene. Taken for reaction were 5.2 g of 1,4-di-β-carboxyethoxybenzene and 24.4 g (14.5 ml) of thionyl chloride. The mixture was heated until the 1,4-di-β-carboxyethoxybenzene dissolved. The excess thionyl chloride was distilled off at atmospheric pressure, traces – in vacuo. The residue was extracted with gasoline. 4.7 g of crystalline product was obtained, m.p. 91-93°, yield 60%.

0.1072 g substance: 0.1047 g AgCl. 0.1254 g substance: 0.1227 g AgCl. Found %: Cl 24.19, 24.25. $C_{12}H_{12}O_4Cl_2$. Calculated %: Cl 24.39.

Cyclization of 1,4-di-β-carboxyethoxybenzene. Taken for reaction were 5 g of di-β-carboxyethoxybenzene, 50 g of phosphoric anhydride, and 100 g of phosphoric acid (s.g. 1.75). The mixture was heated on a water bath for 10 hours. After cooling, the mixture was poured into water and the yellow precipitate filtered off, washed with water, and dried. After one recrystallization from benzene its m.p. was 227-229°; after a second recrystallization its m.p. was 229-230°. Yield 23.2%.

0.0832 g substance: 0.2002 g CO_2; 0.0336 g H_2O. Found %: C 65.62; H 4.48. $C_{12}H_{10}O_4$. Calculated %: C 66.05; H 4.58.

SUMMARY

1. By saponification of 1,2-di-β-cyanoethoxybenzene, 1,3-di-β-cyanoethoxybenzene and 1,4-di-β-cyanoethoxybenzene the corresponding acids were obtained. The full chloranhydrides of 1,3-di-β-carboxyethoxybenzene, 1,4-di-β-carboxyethoxybenzene, and the ethyl ester of 1,3-di-β-carboxyethoxybenzene were obtained.

2. 1,3-Di-β-carboxyethoxybenzene cyclization by phosphoric anhydride was carried out in phosphoric acid medium. A product identical with that of Bachman and Levine was obtained. 1,4-Di-β-carboxyethoxy benzene cyclization by phosphoric anhydride in phosphoric acid medium gives double ring closure.

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SYNTHESIS AND STUDY OF γ-DIETHYLAMINOPROPYL ETHER OF 2-METHOXY-6-ALLYLPHENOL

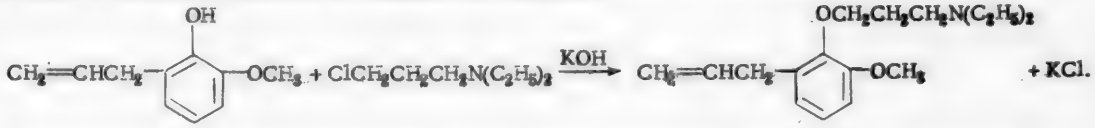
A. M. Khaletsky and T. I. Sokolova

By a series of examples of aromatic compounds with molecules having an unsaturated alkyl radical in the position ortho to phenylhydroxyl, etherified by an alkylamino group, as for example: β-dimethylaminoethyl ether of 2-methoxy-6-allylphenol, β-diethylaminoethyl ether of 2-methoxy-4,6-diallylphenol, β-diethylaminoethylether of 2-methoxy-6-crotylphenol, and β-diethylaminoethyl ether of 1-allylnaphthol – it was shown that such compounds are endowed with hemostatic and uterine activity [1]. Among these compounds the most interesting appeared to be the β-diethylaminoethyl ether of 2-methoxy-6-allylphenol [3], which, under the name of pregnantol or gravitol, in the hydrochloride or citrate form, has found application in medical practice as a replacement for galenic preparations of ergot [2]. It follows therefore, it should be noted, that among the uterine remedies there predominate mostly preparations of vegetative origin (ergot, shepherd purse, snowball tree, water, pepper and others); synthetic preparations, excluding pregnantol, being practically represented by only stiptisin and hydrostinin, obtained by oxidation of narcotin or of hydrastin. The unavailability of hydrastin, and thus the impossibility of obtaining hydrastinin, further reduces the number of synthetic uterine and hemostatic remedies.

The presence, in the pregnantol molecule, of a free radical and alkyl amino group makes it interesting to study this class of compounds for the purpose of demonstrating the relation between their chemical structure and activity. Since the effect of the alkylamino group upon pharmacological activity has been repeatedly on a series of examples (anesthetic p.H., derivatives of acridine [5], and others) one can assume that the physiological action of pregnantol is tied up with this group. To study this dependence we synthesized the nearest analog to pregnantol – the γ-diethylaminopropyl ether of 2-methoxy-6-allylphenol.

By interaction of guaiacol and allyl bromide in the presence of potassium, there was obtained the allyl ether of guaiacol [6] which, upon heating to 240°, isomerized to 6-allylguaiacol [7]. The ease with which the allyl radical passes over from oxygen to carbon [8] was utilized in the present case.

The 6-allylguaiacol synthesized by the authors was reacted further with diethylaminopropyl chloride in the presence of potassium hydroxide, according to the reaction:



Pharmacological tests of the hydrochloride salt and the salt obtained by interaction of the hydrochloride base with the potassium salt of the 1,5-disulfo acid of naphthalene, which were carried out by the Department of Pharmacology of the author's Institute, have less effective uterine action compared with the β-diethyl aminoethyl ether of 2-methoxy-6-allylphenol, which follows because of the lengthening of the alkylamino group chain by a $-CH_2-$.

EXPERIMENTAL

2-Methoxy-6-allylphenol. 120 g of allyl ether guaiacol, obtained by the method of Claison [6], underwent isomerization by heating to 240° for 2 hours, the reaction product being then treated with 60 ml of 5% solution of sodium hydroxide in the presence of 50 ml of ether. The colorless alkaline liquid was neutralized by dilute hydrochloric acid; the precipitated 6-allylguaiacol extracted with ether; the ether liquid washed with water and dried over potassium oxide, and after removal of the ether, fractionated; 80 g of 2-methoxy-6-allylphenol

was obtained, b.p. 120° at 12 mm (76% of the theoretical). For identification of 2-methoxy-6-allylphenol, its allyl ether was synthesized and isomerization to 2-methoxy-6-propylphenol carried out.

16.4 g of 2-methoxy-6-allylphenol was heated with 12.5 g of allyl bromide and 12 g of potash in acetone medium (50 ml) for 6 hours on a water bath. After cooling, water was added to the reaction mixture to dissolve the salts, and the solution obtained was washed with ether after drying of the ether solution by sodium sulfate, then followed by distillation of the ether, the residue, distilled at 130-131°, under 12 mm pressure, yield 16 g (78% of theoretical).

Isomerization of 2-methoxy-6-allylphenol into 2-methoxy-6-propenylphenol was effected by heating 5 g of 2-methoxy-6-allylphenol with 10 g of solid potassium hydroxide in 5 g of water to 170° for 1 hour. The resulting cake was dissolved in water, acidified with hydrochloric acid and washed with ether; the ether solution was dried over anhydrous sodium sulfate, and the ether distilled off. The small amount of residue recovered (2 - 2.5 g) soon crystallized; recrystallized from hot benzene, the substance appeared as long, shiny needles with the odor of oil of cloves, m.p. 76°, corresponding to o-isoeugenole.

γ-Diethylaminopropyl ether of 2-methoxy-6-allylphenol. 44 g of 2-methoxy-6-allylphenol was dissolved in 130 g of 10% potassium hydroxide, and 50 g of 1-diethylamino-3-chloropropane (25% excess) was gradually added, upon which warming up (from 15 to 32°) was observed; subsequently the mixture was heated to boiling on an oil bath at 140-160° for 8 hours. The separated oily layer was extracted with ether. The ether solution was washed with a solution of potassium hydroxide, with water, and then dried over calcium chloride. After removal of the ether, the residue was fractionated; there separated a fraction with b.p. 178-181° at 8 mm pressure in the amount of 55 g (76% theoretical), in the form of a colorless, transparent liquid, insoluble in water, soluble in alcohol, ether, chloroform, benzene, and mineral acids.

0.1495 g substance: 0.4035 g CO_2; 0.1346 g H_2O. 0.1567 g substance: 0.4220 g CO_2; 0.1401 g H_2O. 0.2762 g substance: 10.29 ml 0.1 N. HCl (Kjeldahl). 0.2607 g substance: 9.59 ml 0.1 N. HCl. 0.4231 g substance: 15.30 ml 0.1 N. HCl. 0.3572 g substance: 12.90 ml 0.1 N. HCl. Found %: C 73.61, 73.45; H 10.00, 10.09; N 5.22, 5.15; M 276.6, 276.9. Calculated %: C 73.60; H 9.82; N 5.05; M 277.2. 1.93 mg substance; 4.58 mg camphor: Δt 7° (Rast). Found: M 299.6.

Hydrochloride of γ-diethylaminopropyl ether of 2-methoxy-6-allylphenol. 5 g of γ-diethylaminopropyl ether of 2-methoxy-6-allylphenol was dissolved in 50 g of dry ethyl acetate and the solution saturated with hydrogen chloride; the separated white powder was filtered off and recrystallized from hot ethyl acetate. The salt was soluble in water and alcohol, insoluble in ether and chloroform, m.p. 75-77°.

0.3420 g substance: 12.30 ml 0.1 N. NaOH. 0.3843 g substance: 13.85 ml 0.1 N. NaOH. $C_{17}H_{27}O_2N \cdot HCl$. Found salt %: 99.70, 99.83.

Production of salt from γ-diethylaminopropyl ether of 2-methoxy-6-allylphenol and the 1,5-disulfoacid of naphthalene. 1,5-Disulfoacid of naphalene, produced by sulfonation of naphthalene with 30% oleum; potassium salt separated with a 10% solution of NaCl [9].

5 g of the hydrochloride of the γ-diethylaminopropyl ether of 2-methoxy-6-allyl phenol in 50 ml of water was mixed with a solution of 2.65 g of the potassium salt of the 1,5-disulfoacid of naphthalene; there immediately precipitated needle crystals in clusters, m.p. 120-123° after recrystallization from hot water. The salt is soluble in alcohol, insoluble in ether, and non-hydroscopic, an advantage over the hydrochloride of the same base; 6 g of salt obtained (89% theoretical).

0.2698 g substance: 0.1502 g $BaSO_4$. 0.2597 g substance: 0.1459 g $BaSO_4$. Found %: S 7.65, 7.69. $(C_{17}H_{27}O_2N)_2 \cdot C_{10}H_8O_6S_2$. Calculated %: S 7.61.

SUMMARY

From 2-methoxy-6-allylphenol and 1-diethylamino-3-chloropropane was synthesized the γ-diethylaminopropyl ether of 2-methoxy-6-allylphenol as well as its hydrochloride salt with 1,5-disulfoacid of naphthalene.

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DEHYDRATION AND OXIDATION OF 2-ETHOXY-(5,6,7,8-TETRAHYDRONAPHTHOYL-3)-PROPIONIC ACID

S. I. Sergievskaya and I. M. Lipovich

Upon study of the interaction of α-2-ethoxytetrahydronaphthalene with succinic anhydride, in the presence of $AlCl_3$, S. I. Sergievskaya and A. V. Danilova [1] isolated two isomeric 2-ethoxytetrahydronaphthoylpropionic acids, and demonstrated that the keto acid group, upon condensation, enters into the 3 or the 4 position of the 2-ethoxytetrahydronaphthalene molecule; which one of the two isolated keto acids appears to be 2-ethoxy-(5,6,7,8-tetrahydronaphthoyl-3)- or 2-ethoxy-(5,6,7,8-tetrahydronaphthoyl-4)-propionic acid remained unclarified. In the present work, the authors aim to define more accurately the structure of 2-ethoxytetrahydronaphthoylpropionic acid, m.p. 169-170°, which is formed in large amount.

Upon repeating the above-mentioned reaction for the purpose of obtaining in sufficient amount the acid to be investigated, the reaction conditions and treatment of substance were changed (see Experimental Section), with the result that the keto acid yield was considerably increased, approximately three fold.

To define the structure of the ketoacid, m.p. 169-170°, we first applied the dehydration reaction with the help of 20% palladium on carbon. This method was recommended by Newman and Zahm for the analogous compounds of tetrahydronaphthalene; simultaneously with dehydration of the ring, the carbonyl group is usually reduced to the methylene group.

We proposed to obtain, with the aid of this reaction, 2-ethoxynaphthylbutyric acid, and subsequently, by means of desalkylation, to convert the ethoxyl group, thus to form hydroxynapthylbutyric acid, which could be either 2-hydroxynaphthyl-3- or 2-hydroxynaphthyl-4-butyric acid. A comparison of hydroxynaphthylbutyric acid obtained in this way with that described by G. Val [3], 2-hydroxy-3-naphthylbutyric acid, could resolve the question of the structure of the original ketoacid.

$$\left.\begin{matrix} C_2H_5OC_{10}H_6CO(CH_2)_2COOC_2H_5 \\ C_2H_5OC_{10}H_{10}(CH_2)_3COOC_2H_5 \end{matrix}\right\rightarrow C_2H_5OC_{10}H_6(CH_2)_3COOC_2H_5 \rightarrow C_2H_5OC_{10}H_6(CH_2)_3COOH \rightarrow HOC_{10}H_6(CH_2)_3COOH$$

The ethylesters of both 2-ethoxytetrahydronaphthoylpropionic acid and of 2-ethoxytetrahydronaphthylbutyric acid underwent dehydration (ethoxytetrahydronaphthylbutyric acid is easily obtained from the ketoacid by a Clemmensen reaction).

Dehydration of the ketoacid ester was accompanied by marked resinification, whereas dehydration of the ester of ethoxytetrahydronaphthylbutyric acid under the same conditions proceeds with good results, and thus can be successfully utilized for obtaining exthoxynaphthylbutyric acid. The authors did not succeed in claryifying the structure of the ketoacid by the above method, because the hydroxynaphthylbutyric acid obtained after desalkylation melted at 139-141°, whereas, according to the data of G. Val, 2-hydroxynaphthyl-3-butyric acid melts at 131°. This difference in the melting points can be explained with almost equal probability by either a different degree of purity of the hydroxynaphthylbutyric acids synthesized by different methods, or by the assumption that the hydroxynaphthylbutyric acid obtained by the authors is not 2-hydroxy-3-naphthylbutyric acid, but its isomer.

The indefiniteness of the results obtained compelled the authors to make use of a second possible method for defining the ketoacid structure, namely, its oxidation to ethoxytetrahydronaphthoic acid, followed by desalkylation of the ethoxyl groups. These transformations should lead to some known hydroxytetrahydronaphthoic acids. Oxidation of 2-ethoxytetrahydronaphthoylpropionic acid with the aid of sodium hypochlorite proceeded without any special difficulty, and the same was true of the desalkylation of 2-ethoxytetrahydronaphthoic acid. As the result of these reactions, the substance obtained appeared to be hydroxytetrahydronaphthoic acid, according to the elementary

analysis data, and its melting temperature and other properties were the same as those for 2-hydroxy-3-tetrahydronaphthoic acid, as described in detail by Schroeter [4]. The melting point of the methyl ester of 2-hydroxy-3-tetrahydronaphthoic acid, obtained by the authors, also corresponded precisely with that shown for this compound by Schroeter.

On the basis of these data, the authors conclude that the ketoacid with an m.p. of 169-170° is the 2-ethoxy-(5,6,7,8-tetrahydronaphthoyl-3)-propionic acid.

EXPERIMENTAL

β-(2-Ethoxy-5,6,7,8-tetrahydronaphthoyl-3) propionic acid $C_2H_5OC_{10}H_{10}CO(CH_2)_2COOH$. Into a vessel equipped with a mixer and reflux condenser were placed 85 g of ar-2-ethoxytetralin, 47 g of succinic anhydride, and 1120 ml of absolute nitrobenzene. Then 136 g of aluminum chloride was added in small portions, with mechanical stirring, over a period of 7 to 8 hours. The reaction proceeds at room temperature. The reaction mass was allowed to stand until the following day, when the mixing was continued for five more hours. 1200-1300 ml of water with ice and 340 ml of concentrated sodium chloride were added. A precipitate then settled out, which was filtered and washed with small portions of ether to remove nitrobenzene. 60 g of ketoacid mixture, m.p. 143-147°, was obtained. To the remaining nitrobenzene solution were added ether and a 4 % alkali solution, with shaking. The alkaline solution was separated, and the remainder of the ether removed from it by heating. The alkaline solution was filtered and acidified with 10% hydrochloric acid. The precipitated resinous sediment was sucked off and washed several times with benzene. An additional 30 g of ketone acids mixture, m.p. 130-135°, was obtained.

The isomeric mixtures of 2-ethoxy-(5,6,7,8-)tetrahydronaphthoylpropionic acids were separated according to the method of Sergievskaya and Danilova [1], by their conversion into ethyl esters. After esterification and the usual processing, the mixture of ethyl esters was separated by recrystallization from alcohol; 30 g of the ethyl ester of 2-ethoxytetrahydronaphthoylpropionic acid, m.p. 79-80°, was obtained. After saponification of this ester, 22 g of ketoacid, m.p. 169-170°, was obtained. The residue, m.p. 79-80°, after separation of the ether, was a thick mass, which contained the ethyl ester of the second isomeric acid. This residue was distilled in vacuo. 25 g of a fraction was collected at 225-228° at 4-5 mm. After saponification of this fraction 20 g of substance was obtained. After alcohol recrystallization, 10 g, m.p. 191-192° was obtained, and 10 g with m.p. 154°.

Thus, from 85 g of 2-ethoxytetralin were obtained: 22 g of ketoacid, m.p. 169-170°; 10 g of ketoacid, m.p. 191-192°; and 10 g of ketoacid mixture, m.p. 154°.

Ar-2-Hydroxytetrahydronaphthoyl-3-propionic acid. 10 g of ar-2-ethoxytetrahydronaphthoyl-3-propionic acid, m.p. 169-170°, were dissolved, by heating, in 450 ml of absolute benzene, after which the bath was set aside and 21 g of aluminum chloride added in several stages, and then heated for 5 hours. The benzene was distilled off, up to point of dryness and the residue decomposed with ice and water and 40 ml of concentrated hydrochloric acid. The precipitate was filtered off, and, upon heating, dissolved in 100 ml of 10% alkali solution, with added carbon. The alkali solution was filtered off and acidified with 10% hydrochloric acid. The separated precipitate was filtered off and washed several times with water. 7.5 g of crude substance was obtained. The substance dissolved with difficulty in hot water. After recrystallization from alcohol, the m.p. was 137-140°. Upon second recrystallization from an alcohol-benzene mixture, the m.p. was 139-142°.

For analysis, this ketoacid was further purified by converting to the ethyl ester, recrystallizing the latter, followed by saponification. Purified in this manner the ketoacid, after recrystallization from alcohol, melted at 142-144°.

4.920 mg substance: 12.311 mg CO_2; 2.879 mg H_2O. Found %: C 68.24; H 6.54. $C_{13}H_{16}O_4$. Calculated %: C 67.74; H 6.45.

Ethyl ester of 2-hydroxytetrahydronaphthoyl-3-propionic acid. To 3 g of 2-hydroxytetrahydronaphthoyl-3-propionic acid was added 30 ml of absolute alcohol and 1.7 ml conc. H_2SO_4 and the mixture was heated for 6 hours. The alcohol was distilled off, the residue diluted with water, the separated precipitate filtered off and dissolved in ether, and the ether solution washed with 3% sodium bicarbonate, then with water, and dried with anhydrous sodium sufate; the ether was distilled off and the residue distilled in vacuo. A fraction was collected with b.p. 222-223° at 5-6 mm. The substance quickly crystallized. 2.1 g, m.p. 40-42°, was obtained. After double recrystallization from alcohol, the m.p. was 43.5-45.5°.

4.322 mg substance: 11.041 mg CO_2; 2.893 mg H_2O. Found %: C 69.67; H 7.49. $C_{16}H_{20}O_4$. Calculated %: C 69.56; H 7.24.

γ-(2-Ethoxynaphthyl-3)-butyric acid. a) Dehydration of the ethyl ester of γ-(2-ethoxytetrahydronaphthyl-3)-butyric acid. The ethyl ester of γ-(2-ethoxytetrahydronaphthyl-3)-butyric acid was obtained by a Clemmensen reduction of 2-ethoxytetrahydronaphthoyl-3-propionic acid, with subsequent esterification, was obtained by this method 2-ethoxytetrahydronaphthyl-3)-butyric acid under the conditions indicated by S. I. Sergievskaya and A. V. Danilova.

To 4 g of the ethyl ester of 2-ethoxytetrahydronaphthylbutyric acid, was added 0.5 g of 20% palladium on carbon,* and air was expelled from the apparatus by passing nitrogen through for 10-15 minutes. The bath was heated with Wood's alloy to 200°, the flask with the substances then lowered into the alloy and rapidly brought to a temperature of 270°, at which temperature hydrogen began to evolve.

After 35 minutes 300 ml of hydrogen had been collected, liberation of hydrogen then slowing down. Heating was continued for 1 hour and 45 minutes at a bath temperature of 270-320°. The termination of reaction was judged by the volume of collected hydrogen. Upon cooling, the contents of the flask were dissolved in ether, and removed from the catalyst by filtration. The ether solution was washed was 10 % NaOH and then acidified with 10 % hydrochloric acid. A small precipitate, 0.3 g , separated, m.p. 119-120°.

Ether was distilled off from the ether solution and to the butyrated residue were added 12.3 g KOH and 40 ml of alcohol, and the reaction mixture was heated for 6 hours. After termination of the heating, the alcohol was distilled off, and the remainder diluted with water and acidified with 10% hydrochloric acid. The separated precipitate was filtered off and recrystallized from a mixture of benzene and alcohol. 2.7 g of substance, m.p. 119-121°, was obtained.

3.241 mg substance; 8.830 mg CO_2; 1.966 mg H_2O. Found %: C 74.30; H 6.79. $C_{16}H_{18}O_3$. Calculated %: C 74.42; H 6.97.

b) Dehydration of the ethyl ester of β-(2-ethoxytetrahydronaphthoyl-3)-propionic acid was carried out as in the preceding experiment. 5 g of the ethyl ester of the ketoacid and 0.2 g of 20% palladium on carbon were taken for reaction. Heating was continued for 3.5 hours at 290-310°. After cooling, the contents of the flasks were dissolved in ether, the catalyst filtered off, and the ether solution washed with 10% hydrochloric acid, upon which there separated a resinous precipitate, which was recrystallized from a mixture of benzene and alcohol (more alcohol was taken than benzene). After repeated recrystallizations from benzene, there was obtained 0.2 g of substance, m.p. 119-121°. The earlier-separated ether layer was dried with sodium sulfate. After distillation of the ether, a resinous substance remained, which underwent saponification with alcoholic alkali.

Elementary analysis of the substance with m.p. 119-121° has shown that, by contents, this substance corresponds to 2-ethoxynaphthylbutyric acid.

3.464 mg substance: 9.485 mg CO_2; 2.159 mg H_2O. Found %: C 74.68; H 6.98. $C_{16}H_{18}O_3$. Calculated %: C 74.42; H 6.97.

2-Hydroxy-3-naphthylbutyric acid. Desalkylation of γ-(2-ethoxy-3-naphthyl)-butyric acid, obtained by dehydration of the ethyl ester of γ-(2-ethoxytetrahydronaphthyl-3)-butyric acid followed by saponification of the ethyl ester, was effected in the following manner. 3.5 g of 2-ethoxynaphthyl-3-butyric acid, 70 ml of glacial acetic acid, and 113 ml of 48% hydrobromic acid were heated for 3 hours at 110-125°. After cessation of heat, the mixture was steam evaporated to dryness in vacuo. The residue was dissolved in 10% NaOH, the solution filtered off from the undissolved portion, and the filtrate acidified with 10% hydrochloric acid, the separated acid being filtered off and washed with water. After recrystallization from a benzene-alcohol mixture, 2.3 g of substance, m.p. 138-140°, was obtained. After repeated recrystallization, its m.p. was 139-141°.

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* Preparation of the catalyst. To 5 g of activated wood charcoal were added 10 ml of nitric acid, 1.33, and 100 ml distilled water, and the mixture was heated on a water bath. The acid was then poured off, and the carbon was washed first with hot and then with cold water, and then dried for 8 hours at 100°, and for a few hours at 175-180°.

To 2 g of the charcoal, purified by the indicated method, were added 35 ml of distilled water and 0.8 g of palladium chloride, dissolved by heating in 6 ml of water and 0.5 ml concentrated hydrochloric acid. After passing hydrogen with shaking, into the suspension to the point of discoloration of the liquid, the palladium was filtered off, washed first with hot distilled water and then with cold until there was no chloride in the wash water, then subsequently with alcohol, ether, and finally dried in a vacuum dessicator over alkali.

4.173 mg substance: 11.159 mg CO_2; 2.200 mg H_2O. 3.995 mg substance: 10.680 mg CO_2; 2.198 mg H_2O. Found %: C 72.93, 72.91; H 6.17, 6.15. $C_{14}H_{18}O_3$. Calculated %: C 73.04. H 6.09.

Upon desalkylation of 2-ethoxy-3-naphthylbutyric acid, which was obtained by dehydration of the ethyl ester of 2-ethoxytetrahydro-3-naphthoylpropionic acid with subsequent saponification of the ester, there was taken 0.2 g of 2-ethoxy-3-naphthylbutyric acid, 4 ml of glacial acetic acid, and 6.5 ml of 48% hydrobromic acid. After the usual treatment and recrystallization of the separated substance, its m.p. was 139-141°. The analytical data corresponded to the composition of hydroxynaphthylbutyric acid.

4.432 mg substance: 11.960 mg CO_2; 2.359 mg H_2O. Found %: C 73.59; H 5.95. $C_{16}H_{16}O_3$. Calculated %: C 73.04; H 6.09.

Ethyl ester of γ-(2-hydroxynaphthyl-3)-butyric acid. To 1.8 g of γ-(2-hydroxynaphthyl-3)-butyric acid were added 20 ml of absolute alcohol, 1 ml of concentrated sulfuric acid, and the mixture was heated for 6 hours. After completion of the reaction, the alcohol was distilled off, the residue diluted with water and extracted with ether, and the ether solution washed with 3% aqueous sodium bicarbonate, then with water, and dried with sodium sulfate. After removal of the ether, 1.5 g of precipitate was obtained from the small volume remaining; after double recrystallization from petroleum ether, the m.p. of the substance was 70-71°.

3.850 mg substance: 10.498 mg CO_2; 2.329 mg H_2O. Found %: C 74.37; H 6.77. $C_{16}H_{18}O_3$. Calculated %: C 74.42; H 6.97.

Oxidation of β-(2-ethoxytetrahydronaphthoyl-3)-propionic acid. ar-2-Ethoxy-3-tetrahydronaphthoic acid. 18 g of sodium hydroxide dissolved in 30 ml of water was placed into an ice-cooled flask; into this alkaline solution was passed chlorine to an excess weight of 12 g. The resultant sodium hypochlorite solution was heated to 50°, with mechanical stirring, and to it was gradually added 2 g of β-(2-ethoxytetrahydronaphthoyl-3)-propionic acid dissolved in 15 ml of 40% sodium hydroxide solution. After addition of the ketoacid, stirring and heating were continued for 3 hours at 70°. The reaction mixture was left overnight and then the precipitated sodium salt of 2-ethoxytetrahydronaphthyl-3-carboxylic acid was filtered off. To the substance obtained was added water, and to the suspension was added, with thorough mixing, 10% hydrochloric acid to the point of acid reaction to Congo. The separated substance was filtered off and recrystallized three times from alchohol. Yield 0.6 g with m.p. 118-120°.

3.875 mg substance: 10.045 mg CO_2; 2.496 mg H_2O. Found %: C 70.56; H 7.20. $C_{13}H_{16}O_3$. Calculated %: C 70.80; H 7.27.

Desalkylation of ar-2-ethoxytetrahydro-3-naphthoic acid. Ar-2-Hydroxy-3-tetrahydronaphthoic acid. To 1.7 g of 2-ethoxytetrahydronaphthoic acid were added 34 ml of glacial acetic acid and 55 ml of 48% hydrobromic acid. The reaction mixture was heated for 3 hours at 110-125° and evaporated to dryness in vacuo. The residue was dissolved in 10% NaOH solution, filtered off from the undissolved portion, and the filtrate acidified with 10% hydrochloric acid. 12 g of substance was obtained, m.p. 176-179°. After double recrystallization from a benzene-alcohol mixture, its m.p. was 181-182°. *

3.671 mg substance; 9.191 mg CO_2; 2.080 mg H_2O. Found %: C 68.28; H 6.33. $C_{11}H_{12}O_3$. Calculated %: C 68.75; H 6.25.

Methyl ester of 2-hydroxy-3-tetrahydronaphthoic acid. To 0.6 g of 2-hydroxytetrahydro-3-naphthoic acid were added 10 ml of absolute methanol, 0.5 ml of concentrated sulfuric acid, and the mixture heated for 6 hours. The alcohol was then distilled off; the remainder was diluted with water and treated with ether; the ether solution was washed with 3% sodium bicarbonate solution, then with water, and dried with sodium sulfate. The ether was distilled off. The residue was recrystallized from alcohol, m.p. 41-42.5°. According to Schroeter, the m.p. of the methyl ester of 2-hydroxytetrahydro-3-naphthoic acid was 42°.

4.245 mg substance: 10.886 mg CO_2; 2.556 mg H_2O. Found %: C 69.93; H 6.73. $C_{12}H_{14}O_3$. Calculated %: C 69.90; H 6.84.

SUMMARY

1. The structure of 2-ethoxy-(5,6,7,8)-tetrahydronaphthoyl-3-propionic acid has been defined more accurately by its oxidation to 2-ethoxy-3-tetrahydronaphthoic acid and by further transformation of the latter into compounds of

* 2-Hydroxy-3-tetrahydronaphthoic acid was obtained by Schroeter using other methods. The indicated m.p. in one instance was 176-177°, in another, 182°.

already established structure.

2. Dehydration of the ethyl ester of 2-ethoxy-(5,6,7,8)-tetrahydronaphthyl-3-butyric acid was carried out in the presence of palladium on carbon.

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MESO ANTHRANILPROPIONIC ACIDS

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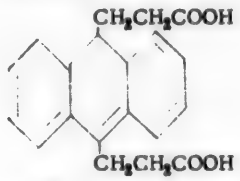
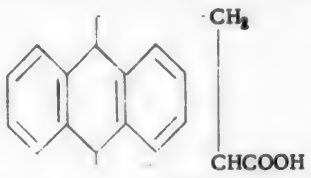
In 1940, A. G. Slobodsky and V. I. Khmelevsky [1] reported that attempts to synthesize β,β'-(anthranil-9,10)-dipropionic acid (I) by heating anthracene with acrolein, with subsequent oxidation, yielded, instead, α,β-endo-(9,10-dihydroanthranil-9,10)-propionic acid (II). The authors indicated that this reaction takes place only in the presence of SO_2, and that all attempts to connect acrolein with anthracene in the absence of sulfurous acid were unsuccessful. (This appeared to be a singular observation, because it is known [2] that the presence of SO_2



(I)

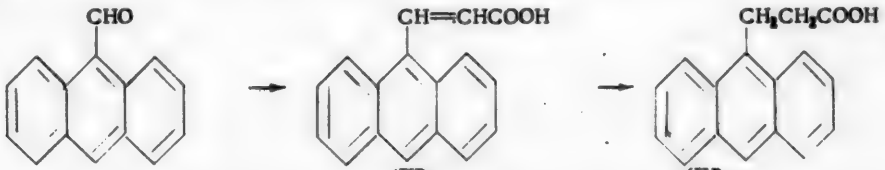


(II)

as a catalyst is indispensable only when acrolein condenses with compounds that possess sufficiently reactive hydrogen atoms, as the result of which condensation are formed β-substituted derivatives of propionic aldehyde.) On the contrary, in diene synthesis in which acrolein participates, as in the example under investigation where acrolein and anthracene interact with the formation, after oxidation, of endodihydroanthranilpropionic acid (II), the presence of a catalyst is usually unnecessary. Indeed, acid (II) is also easily obtained by heating anthracene with acrylic acid or, even more conveniently with β-halogen-propionic acid [3].

The author conducted experiments involving condensation of anthracene with acrolein under the conditions described by Slobodsky and Khmelevsky, both with and without the presence of SO_2 catalyst, demonstrating that the presence of sulfurous acid does not play an essential role in this reaction. In both instances, after oxidation of the reaction product with silver oxide in alkaline medium, there was isolated one and the same α,β-endo-(9,10-dihydroanthranil-9,10)-propionic acid, identical with the acid obtained by heating anthracene with β-bromopropionic acid in cymene.

If anthracene reacted with acrolein in such a way that one atom of hydrogen in the meso position, and the anthracene residue, added to the double bond of acrolein, then oxidation of the reaction product should yield a substance isomeric with acid (II) – β-(anthranil-9)-propionic acid (IV). For confirmation of the structure of the acrolein interaction product, this acid, not described in the literature, was synthesized by the author according to the following scheme:



(III) (IV)

Upon condensation of 9-anthraldehyde with acetic anhydride in the presence of potassium acetate, there was obtained β-(anthranil-9)-acrylic acid (III) in the form of yellow needles, m.p. 246-247°. It is worthy of attention that in the presence of freshly melted sodium acetate there is almost no formation of acid (III).

It is of interest to note that the few literature references to β-(anthranil-9)-acrylic acid are extremely contradictory. Davis and Carmack [4], as a result of condensation of 9-anthraldehyde with malonic acid, obtained 9-anthralmalonic acid, m.p. about 145°, which easily decarboxylated at 180-190° to form β-(anthranil-9)-acrylic acid. The latter, identical with the one synthesized by the author, had an m.p. of 246-247°. Contrariwise, Fieser

and Hartwell [5], also condensing 9-anthraldehyde with malonic acid, obtained only the acid with m.p. 240-246°, to which they attributed the structure of 9-anthralmalonic acid. The authors were unable to decarboxylate this acid, despite many attempts on their part. Judging from the m.p. of the obtained substance and its unusual resistance to decarboxylation, it can be assumed that, under the conditions of condensation of 9-anthraldehyde with malonic acid, decarboxylation occurred simultaneously, as the result of which Fieser and Hartwell obtained not anthralmalonic acid, but β-(anthranil-9)-acrylic acid. However, this normal assumption is contradicted by the data quoted in the article by the mentioned authors for the analysis of both the acid proper and its "dimethyl" ester, m.p. 134.5-135.5°. It should be noted that the methyl ester of β-(anthranil-9)-acrylic acid obtained by the present author had an m.p. of 110-111°. All of these data permit expression of serious doubt as to the reliability of the result obtained by Fieser and Hartwell.

As a result of reduction of β-(anthranil-9)-acrylic acid with sodium amalgam in aqueous medium, there was obtained β-(anthranil-9)-propionic acid (IV) in the form of thick yellow crystals, m.p. 190-191°.

The presence of color, as a rule, is characteristic for mesoderivatives of anthracene of this type, while the endo compounds of type (II) are usually colorless. In addition to this distinctive characteristic of β-(anthranil-9)-propionic acid, as well as that of β-(anthranil-9)-acrylic acid, is the fact that their sodium salts in aqueous solution are very susceptible to the action of oxygen of the air. Upon standing, these solutions become turbid comparatively quickly as the result of oxidation and formation of anthraquinone. The same phenomenon is observed among other analogous derivatives of anthracene, for example in the case of the sodium salt of anthracene-9-carboxylic acid [6]. On the contrary, the aqueous solution of the sodium salt of α,β-endo-(9,10-dihydroanthranil-9,10)-propionic acid is stable and remains colorless upon storage.

EXPERIMENTAL

α,β-Endo-(9,10-dihydroanthranil-9,10)-propionic acid (II).

a) Condensation of anthracene with acrolein. A mixture of 2 g of pure anthracene and 2 g of acrolein, stabilized by hydroquinone, was heated in a sealed tube for 3 hours at 130°. After completion of the reaction, the yellow-brown liquid was diluted with a small volume of alcohol and poured into five times the volume of water. To the formed emulsion was added a solution of 6 g of silver nitrate in 25 ml of water, followed by 30 ml of 10% sodium hydroxide solution. The mixture was heated and the precipitate filtered off and washed with hot water. The filtrate, together with the wash waters, was shaken with ether for the removal of the neutral admixtures, and after separation of the ether layer was acidified with hydrochloric acid to the point of acidity to Congo. A yellowish precipitate settled out, weight 0.3 g, and was purified by reprecipitation from alkaline solution and animal charcoal. After recrystallization from 50% methanol, colorless crystals were obtained, m.p. 187-188°. The presence of 1 drop of aqueous sulfurous acid, containing 1 mg SO_2, did not affect the result. The yield of crude acid was 0.55 g.

3.317 mg substance: 9.916 mg CO_2; 1.668 mg H_2O. Found %: C 81.53; H 5.63. $C_{17}H_{14}O_2$. Calculated %: C 81.6; H 5.6.

b) Condensation of anthracene with β-bromopropionic acid. A mixture of 0.89 g of anthracene, 1.15 g of β-bromopropionic acid and 3.0 ml of p-cymene was heated at boiling for 7 hours. Upon cooling, the mixture was diluted with ether and extracted with 3% potassium hydroxide solution. The alkaline solution was refiltered and acidified to the acid point with Congo. The separated precipitate was filtered off, washed, and recrystallized from 50% methanol. Colorless crystals, m.p. 187-188°. A sample mixed with the acid obtained by condensing anthracene with acrolein did not exhibit a lowered m.p.

The sodium salt of α,β-endo-(9,10-dihydroanthranil-9,10)-propionic acid crystallizes out of water as long, flat, colorless needles with a satin sheen, containing 6 molecules of water of crystallization.

0.8756 g substance: 0.2467 g loss in weight at 105°; 0.1596 g Na_2SO_4. Found %: H_2O 28.17; Na 5.91. $C_{17}H_{13}O_2Na \cdot 6H_2O$. Calculated %: H_2O 28.4; Na 6.05.

An aqueous solution of the salt remains clear upon standing.

β-(Anthranil-9)-acrylic acid (III)

A mixture of 10 g of 9-anthraldehyde [7], 10 g of acetic anhydride and 5 g of freshly fused potassium acetate was heated with reflux for four hours at 150-160° bath temperature. The reaction mixture was poured into ice water, the precipitate separated, finely pulverized, and washed with water. Upon heating with sodium carbonate, the substance partially dissolved with the formation of a vivid orange solution, which was refiltered and acidified to the

acid point of Congo. A bright yellow precipitate was separated, washed with water and dried. Weight was 6 g. After double recrystallization from propionic acid, yellow needles, m.p. 246-247°, were obtained.

2.712 mg substance: 8.210 mg CO_2; 1.156 mg H_2O. Found %: C 82.46; H 4.77. $C_{17}H_{12}O_2$. Calculated %: C 82.3; H 4.84.

As the result of condensation of anthraldehyde with acetic anhydride, in the presence of freshly fused sodium acetate and a few drops of pyridine, with heating for 9 hours at 160-170°, there separated only about 0.5 g of crude acid.

The sodium salt of β-(anthranil-9)-acrylic acid crystallized from water in the form of orange lamellae. They contained 4 molecules of water of crystallization.

1.1912 g substance: 0.2469 g loss in weight at 105°; 0.2500 g Na_2SO_4. Found %: H_2O 20.73; Na 6.80. $C_{17}H_{11}O_2Na \cdot 4H_2O$. Calculated %: H_2O 21.05; Na 6.73.

Upon recrystallization from alcohol, the sodium salt separated in the form of long yellow needles with 1 molecule of alcohol of crystallization.

1.3488 g substance: 0.1974 g loss in weight at 105°; 0.2964 g Na_2SO_4. Found %: C_2H_5OH 14.64; Na 7.12. $C_{17}H_{11}O_2Na \cdot C_2H_5OH$. Calculated %: C_2H_5OH 14.56; Na 7.28.

An aqueous solution of the salt upon standing rapidly became turbid as the result of oxidation and formation of anthraquinone.

The methyl ester of β-(anthranil-9)-acrylic acid was obtained by the action of dimethylsulfate upon the alkaline solution of the acid. After double recrystallization from acetic acid – bright yellow needles, m.p. 110-111°.

3.246 mg substance: 9.833 mg CO_2; 1.622 mg H_2O. Found %: C 82.62; H 5.59. $C_{18}H_{14}O_2$. Calculated %: C 82.4; H 5.34.

β-(Anthranil-9)-propionic Acid (IV)

To a suspension of 3 g of β-(anthranil-9)-acrylic acid in 500 ml of water, with vigorous stirring was gradually added 50 g of 2.5% sodium amalgam. After completion of the reaction the aqueous solution was filtered and acidified, whereupon there separated a voluminous yellow precipitate. The precipitate was separated, washed with water, dried (weight 2.4 g) and recrystallized several times from acetic acid. Dense, bright yellow crystals, m.p. 190-191°.

4.860 mg substance: 14.510 mg CO_2; 2.464 mg H_2O. 0.2249 g substance: 9.0 ml 0.1 N. NaOH. Found %: C 81.42; H 5.63; M 249.9. $C_{17}H_{13}O_2$. Calculated %: C 81.6; H 5.60; M 250.

From the mother liquor was separated a small amount of anthraquinone, evidently formed by the action of oxygen upon the alkaline solution of the acid.

The sodium salt of β-(anthranil-9)-propionic acid crystallizes from water in the form of pale yellow needles, an aqueous solution of this salt, upon standing, rapidly becomes turbid, but if freshly boiled water is used and the solution kept under nitrogen, it will remain clear.

SUMMARY

1. It has been shown that condensation of anthracene with acrolein, carried out in accordance with the diene- type of synthesis, does not require the presence of sulfurous acid as catalyst.

2. β-(Anthranil-9)-acrylic acid and β-(anthranil-9)-propionic acids and some of their derivatives have been synthesized and characterized.

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SOME SYNTHESES IN THE 4-ACETAMINOBENZALDEHYDE SERIES

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Of numerous synthetic compounds possessing antitubercular activity, which have been studied over the past years, of great interest are the thiosemicarbazones of aromatic aldehydes, and in particular, the thiosemicarbazone of 4-acetaminobenzaldehyde [1,2]. This compound has already been introduced into the medical practice [3,4] of several countries. In this connection it is of great interest to obtain a series of other derivatives of aminobenzaldehyde, among them those with substitutions in the aromatic ring.

To obtain 2- and 3-substituted para-aminobenzaldehydes, it is most convenient to utilize the reaction of oxidation-reduction , which results in 2- and 3- substituted paranitrotoluenes by interaction in an alcoholic solution of alkaline sulfide. By this method, for example, are easily obtained 2- and 3-methoxy-4-aminobenzaldehydes, 2-chlor-4-aminobenzaldehyde and a series of others [5,6], but this reaction does not proceed in the presence of the hydroxyl or the amino group in the 2-position, which is free or easily freed by hydrolysis. In the last case, almost complete reduction of the nitro group to the amino group is observed. In the case of 2-benzyl-hydroxy-nitrotoluene, only a small amount of 2-benzylhydroxy-4-aminobenzaldehyde is obtained by interaction with alkaline sulfide. The main direction of the reaction apparently being that of reduction to substituted paratoluidine. To obtain substituted 4-aminobenzaldehyde, with a second amino group in the ring, nitration of 4-acetamino-3-nitrobenzaldehyde was carried out, according to Cohn and Springer [7], and the 4-acetamino-3-nitrobenzaldehyde obtained was reduced catalytically to 4-acetamino-3-aminobenzaldehyde, from which was obtained 3,4-diacetaminobenzaldehyde.

From 2- and 3-methoxy-4-aminobenzaldehydes were prepared their succinyl- and benzoyl-amino derivatives. From these aldehydes were obtained the thiosemicarbazones.

2-Methoxy-4-acetaminobenzaldehyde served for the authors as the starting material for the synthesis of 2-hydroxy-4-aminohydrocinnamic acid, which is of interest as a homolog of para-aminosalicylic acid – a substance endowed with high antitubercular activity. 2-Methoxy-4-acetaminobenzaldehyde was condensed with malonic acid in the presence of alcoholic ammonia, and after decarboxylation there was obtained 2-methoxy-4-acetaminocinnamic acid, which was hydrogenated in the presence of elementary nickel catalyst, and the resulting 2-methoxy-4-acetaminohydrocinnamic acid, after boiling with 48% hydrobromic acid, in glacial acetic acid, was converted to 2-hydroxy-4-aminohydrocinnamic acid.

EXPERIMENTAL

4-Acetamino-2-methoxybenzaldehyde. To 10 g of the methyl ether of 4-nitro-2-cresol in 40 ml of alcohol, there was added, over a period of three hours of boiling a solution of 6 g of sulfur in 85 ml of 12% aqueous sodium hydroxide. After one hour of heating, the alcohol and water were vaporized off by steam. Upon cooling, the separated 4-amino-2-methoxybenzaldehyde was filtered off and then treated with 5% hydrochloric acid. The hydrochloride of 4-amino-2-methoxybenzaldehyde obtained was acetylated with acetic anhydride in the presence of sodium acetate and glacial acetic acid. The 4-acetamino-2-methoxybenzaldehyde, recrystallized from water, had an m.p. of 143-144° (m.p. is 145° according to the literature).

4-Amino-2-methoxybenzalthiosemicarbazone, m.p. 163-164° (from alcohol).

4.907 mg substance: 5.192 mg $BaSO_4$. Found %: S 14.35. $C_9H_{12}ON_4S$. Calculated %: S 14.27.

4-Acetamino-2-methoxybenzalthiosemicarbazone, after recrystallization from alcohol, had an m.p. of 211-212°.

4.372 mg substance: 3.859 mg $BaSO_4$. Found %: S 12.12. $C_{11}H_{14}O_2N_4S$. Calculated %: S 12.02.

4-Acetamino-2-benzylhydroxybenzaldehyde. To 12 g of the benzylether of 4-nitro-2-cresol in 50 ml of

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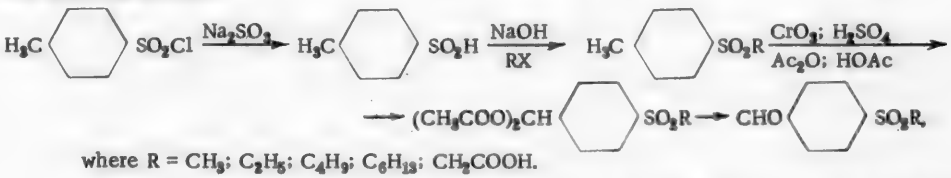
THE SYNTHESIS OF CERTAIN p-ALKYLSULFONYLBENZALDEHYDES

M. N. Shchukina and T. P. Sycheva

As is known, the oxidation of p-nitrotoluene with chromic anhydride, in the presence of glacial acetic acid, acetic anhydride and concentrated sulfuric acid, yields p-nitrobenzaldehyde [1]. Lately it has been determined that in a similar manner the oxidation of certain aryl-p-tolylsulfones yields p-arylsulfonylbenzaldehydes [2]. The outstanding advantage of this reaction appears to be the fact that the reaction stops at the aldehyde stage, because, at the rate of formation of the latter, there occurs transformation into the diacetate, which is resistant to further oxidation. Up to the present, however, it has remained unclarified whether if this method is applied to the oxidation of alkyl-p-tolylsulfones, the action of the oxidizer in this case will be mainly directed upon the methyl group of the tolyl radical, or whether the aliphatic sulfone radical will be seriously affected.

A series of experiments conducted by the authors has indicated that this method is fully applicable for the preparation of p-alkylsulfonylbenzaldehydes [3]. Of this series of compounds, up to now there has been described only p-methylsulfonylbenzaldehyde, obtained in 1945 [4] from acetanilide in 7 steps, the last of which consisted of transforming p-methylsulfonylbenzonitrile into the aldehyde by the action of anhydrous lead chloride in ether solution.

The course worked out by the authors for synthesis of the alkylsulfonylbenzaldehyde series is expressed by the following scheme:



where R = CH_3; C_2H_5; C_4H_9; C_6H_{13}; CH_2COOH.

p-Toluene sulfochloride, by sodium sulfite reduction at 60-80°, was transformed into p-toluenesulfinic acid [5] with a yield of 98% of theoretical. By condensing the sodium salt of this acid with alkyl halides in water-alcohol medium, with 16-22 hours heating, the corresponding alkyl-p-tolylsulfones were obtained, which underwent oxidation with excess chromic anhydride in a mixture of glacial acetic acid, acetic anhydride and concentrated sulfuric acid. The reaction was carried out with cooling and with vigorous stirring so that the temperature would not exceed +5° to +9°, for otherwise the yield of aldehyde was reduced. Treatment with aqueous acetic acid frequently led to the formation of resinous chromic complexes, which also resulted in considerable reduction of yield.

The great advantage of the method given for obtaining alkylsulfonylbenzaldehydes is the fact that alkyl-p-tolylsulfones can undergo oxidation without prior purification, since the major part of the admixture separates easily during the course of the reaction.

Upon pouring the reaction mass into ice water, the diacetates of the aldehydes separate out in the form of colorless crystalline compounds, with the exception of the p-hexylsulfonylbenzaldehyde diacetate which comes out as an oily liquid. After saponification of the aldehyde diacetates withsulfuric acid in water-alcohol medium, the free aldehydes obtained were: p-methyl-, p-ethyl-, p-butyl- and p-hexyl-sulfonylbenzaldehydes. For their characterization, the corresponding thiosemicarbazones were prepared.

Upon oxidation, under analogous conditions, of p-tolylsulfonylacetic acid, there was obtained benzaldehyde-p-sulfonylacetic acid – p-carboxymethylsulfonylbenzaldehyde. It is of interest to note that upon carrying out the condensation of the sulfinic acid sodium salt with chloracetic acid, there separated out of the mother liquor from p-tolylsulfonylacetic acid a crystalline substance which was found to be p,p'-ditolyldisulfoxide [7]. Both the diacetate of p-carboxymethylsulfonylbenzaldehyde and the aldehyde itself represent non-crystallizing substances. It was impossible to obtain the aldehyde in completely pure form since it easily decomposes upon heating. For characterization of this aldehyde, the thiosemicarbazone was made.

EXPERIMENTAL

Hexyl-p-tolylsulfone. A mixture of 16 g p-toluenesulfinic acid with 40 ml of water was neutralized with 10% NaOH solution to a weak alkaline reaction to methyl red indicator, and to the solution were added 90 ml of alcohol and 17 ml of hexyl bromide. The mixture was boiled on a water bath for 23 hours, and the solvent then removed by distillation; water was added to the remainder, and the separated light yellow oil was extracted with ether. The ether solution was washed with water and dried with potash. There remained, after distillation of the ether, a yellowish mobile liquid, hexyl-p-tolylsulfone, which was redistilled in vacuo; b.p. 158-159° at 0.8 mm. Yield 16 g.

0.1955 g substance: 0.1897 g $BaSO_4$. Found %: S 13.32. $C_{13}H_{20}O_2S$. Calculated %: S 13.33.

Oxidation of methyl-p-tolylsulfone. To the solution of 11.48 g methyl-p-tolylsulfone (obtained by the condensation of the sodium salt of p-toluenesulfinic acid with methyl iodide [8]) in 106 ml glacial acetic acid and 105 ml acetic anhydride, with ice cooling and rapid stirring, 15.8 ml of concentrated sulfuric acid was added dropwise at such a rate that the temperature did not exceed +10°. To the reaction mixture was further added slowly, with cooling and stirring, 19 g of dry powdered chromic anhydride at a temperature from +7° to +9°, after which the mixing was continued for 10-15 minutes. The reaction mixture was poured onto 600 g of ice, and to the mixture was added 400 ml of water. The separated precipitate was filtered off, washed with ice water, and with vigorous stirring was treated with 50 ml of 2% sodium bicarbonate; the precipitate was further washed with water and dried in a vacuum dessicator.

Yield of the p-methylsulfonylbenzaldehyde diacetate was 9.44 g. After recrystallization from 96% alcohol, its m.p. was 135-137°.

4.100 mg substance: 7.557 mg CO_2; 1.882 mg H_2O. Found %: C 50.27; H 5.13. $C_{12}H_{14}O_6S$. Calculated %: C 50.33; H 4.93.

p-Methylsulfonylbenzaldehyde. A mixture of 8 g of the diacetate of p-methylsulfonylbenzaldehyde, 15.5 ml of water, 15.5 ml of alcohol and 1.55 ml of concentrated sulfuric acid was boiled on a water bath for 1 hour. At the end of the heating period all of the diacetate precipitate was dissolved. To the solution was further added a small amount of activated carbon, and heating continued for another 5-10 minutes. The hot solution was filtered and cooled with ice water. The separated crystals of p-methylsulfonylbenzaldehyde, after suction filtration, were washed with dilute alcohol and dried in a vacuum dessicator.

Yield 3.25 g. After recrystallization from aqueous alcohol, the substance had an m.p. of 156-158° (according to the literature, 157° [4]).

Thiosemicarbazone of p-methylsulfonylbenzaldehyde – almost colorless crystals; m.p. 232° (with decomposition).

0.2117 g substance: 0.3672 g $BaSO_4$. Found %: S 25.00. $C_9H_{11}O_2N_3S_2$. Calculated %: S 24.90.

Oxidation of ethyl-p-tolylsulfone. To a solution of 5.5 g of ethyl-p-tolylsulfone (obtained by condensation of the sodium salt of p-toluenesulfinic acid with ethyl bromide [9]) in a mixture of 47.5 ml of glacial acetic acid and 47 ml of acetic anhydride there was gradually added 7.1 ml of concentrated H_2SO_4 at a temperature not exceeding +10°. Then 8.5 g of chromic anhydride was gradually added. The experiment was carried out under the same conditions as was shown above for the oxidation of methyl-p-tolylsulfone. After treatment of the reaction mixture there was separated 5 g of p-ethylsulfonylbenzaldehyde diacetate (yield 56% of theoretical). Recrystallized from alcohol, the substance had an m.p. of 107-108°.

2.876 mg substance: 5.499 mg CO_2; 1.378 mg H_2O. Found %: C 52.15; H 5.36. $C_{13}H_{16}O_6S$. Calculated %: C 52.00; H 5.33.

p-Ethylsulfonylbenzaldehyde. A mixture of 5 g of the diacetate of p-ethylsulfonylbenzaldehyde, 10.4 ml of alcohol, 10.4 ml of water and 1.04 ml of concentrated sulfuric acid was boiled on a water bath for 0.5 hours. After treatment with carbon, followed by filtration and cooling, there separated 2.66 g of p-ethylsulfonylbenzaldehyde with an m.p. of 105-106.5°. Yield 82% of theoretical.

For the purpose of analysis the substance was recrystallized from 30% alcohol.

3.404 mg substance; 6.840 mg CO_2; 1.471 mg H_2O. Found %: C 54.80; H 4.83. $C_9H_{10}O_3S$. Calculated %: C 54.54; H 5.05.

Thiosemicarbazone of p-ethylsulfonylbenzaldehyde – light yellow crystals; m.p. 223-224°.

4.175 mg substance: 7.150 mg $BaSO_4$. 6.175 mg substance; 0.825 ml N_2 (17°, 733 mm). Found %: S 23.51; N 15.16. $C_{10}H_{12}O_2N_3S_2$. Calculated %: S 23.34; N 15.50.

Oxidation of butyl-p-tolylsulfone. To a solution of 8 g of butyl-p-tolylsulfone (obtained by condensation of the p-toluenesulfinic acid sodium salt with butyl bromide [10]) in a mixture of 57 ml of glacial acetic acid and 58 ml of acetic anhydride there was gradually added 8.5 ml of concentrated sulfuric acid and then 11 g of chromic anhydride. The experiment was carried out under the above-described conditions. After the usual treatment there was isolated 6.57 g of p-butylsulfonylbenzaldehydediacetate; recrystallized from alcohol, the substance had an m.p. of 106-108°.

3.951 mg substance: 7.933 mg CO_2; 2.229 mg H_2O. Found %: C 54.76; H 6.31. $C_{15}H_{20}O_6S$. Calculated %: C 54.87; H 6.09.

p-Butylsulfonylbenzaldehyde. A mixture of 6 g of p-butylsulfonylbenzaldehydediacetate, 10 ml of alcohol, 10 ml of water and 1 ml of concentrated sulfuric acid was boiled on a water bath for 1 hour. Upon cooling there separated from the solution an oil. The mixture was poured into water, extracted with ether, the ether solution washed with water and dried with sodium sulfate. The residue, after removal of the solvent was found to be a difficultly-crystallizable oily liquid, giving a characteristic aldehyde reaction with ammoniacal silver solution.

Upon mixing an alcoholic solution of this aldehyde with a hot aqueous solution of thiosemicarbazide, there was obtained the semicarbazone, m.p. 184-185°.

0.0744 g substance: 0.1148 g $BaSO_4$. Found %: S 21.19. $C_{12}H_{17}O_2N_3S_2$. Calculated %: S 21.39.

Oxidation of hexyl-p-tolylsulfone. To a solution of 13 g of hexyl-p-tolylsulfone in a mixture of 85 ml acetic anhydride and 85.5 ml of glacial acetic acid, there was added 13 ml of concentrated sulfuric acid, and later, 15 g of chromic anhydride. The reaction was carried out under the above-shown conditions. After completion of the chromic anhydride addition, the reaction mixture was stirred for another 10-15 minutes at room temperature and then was poured into 1 liter of water containing ice. Immediately an oil separated which did not crystallize. The substance was extracted with ether, the ether solution then washed several times with water, and with excess of bicarbonate dissolved in water, to remove the acetic acid and then dried with calcined potash. After distillation of the solvent, the residue was in the form of a yellow, oily liquid with a sharp odor. Weight 11 g. Even after considerable cooling, the substance did not crystallize.

p-Hexylsulfonylbenzaldehyde. A mixture of 11 g of p-hexylsulfonylbenzaldehyde diacetate obtained from an earlier experiment, 40 ml of alcohol, 15 ml of water and 1.8 ml of concentrated sulfuric acid was boiled on a water bath for 1 hour; the alcohol was then distilled off in vacuo, and water was added to the residue. The separated oil was extracted with ether, the ether solution washed with water and dried with anhydrous sodium sulfate. After distilling off the solvent, the residue (9.7 g) was redistilled in vacuo.

p-Hexylsulfonylbenzaldehyde appears in the form of a viscous, colorless liquid, m.p. 151-152° at 0.3 mm.

0.1667 g substance: 0.1529 g $BaSO_4$. Found %: S 12.59. $C_{13}H_{18}O_3S$. Calculated %: S 12.54.

Thiosemicarbazone – slightly yellowish crystals, m.p. 182-184°.

0.1266 g substance: 0.1781 g $BaSO_4$. Found %: S 19.34. $C_{14}H_{27}O_2N_3S_2$. Calculated %: S 19.45.

Oxidation of p-tolylsulfonylacetic acid. To a solution of 7.7 g of p-tolylsulfonylacetic acid (obtained by condensation of monochloracetic acid with p-toluenesulfinic acid [6]) in a mixture of 57 ml glacial acetic acid and 56.5 ml of acetic anhydride was added dropwise, with cooling and stirring, 8.5 ml of concentrated sulfuric acid, followed by 11 g of chromic anhydride at a temperature from +6 to +8°. Upon completion of the chromic anhydride addition, the mixture was poured into 600 g of water with ice. The aqueous solution was extracted several times with ether, the ether extracts dried with anhydrous sodium sulfate; the ether and acetic acid were removed in vacuo. The remaining non-crystallizable oily liquid (6.82 g) was dissolved in 11 ml of alcohol, and to the solution was added 11 ml of water and 1.1 ml of concentrated sulfuric acid. After heating the mixture on a water bath for 1 hour, the alcohol and the ethyl acetate formed were removed by distillation; to the remainder was added water, and the separated oil extracted with ether. The ether solutions were twice washed with water, dried with anhydrous sodium sulfate and the solvent removed in vacuo. The residue – benzaldehyde-p-sulfonylacetic acid – appeared as a yellow oily-like liquid, giving a characteristic aldehyde reaction with ammoniacal silver solution, and was dissolved in bicarbonate. When an attempt was made to distill it in vacuo, the substance decomposed.

Thiosemicarbazone of benzaldehyde-p-sulfonylacetic acid – yellowish crystals, soluble in bicarbonate; m.p. 228-229°.

0.1107 g substance: 0.1709 g $BaSO_4$. Found %: S 21.19. $C_{10}H_{11}O_4N_3S_2$. Calculated %: S 21.40.

SUMMARY

A method for the preparation of p-alkylsulfonylbenzaldehydes has been worked out, consisting of the oxidation of alkyl-p-tolylsulfones by chromic anhydride in the presence of glacial acetic acid, acetic anhydride and concentrated sulfuric acid.

A series of p-alkylsulfonylbenzaldehydes and their derivatives was obtained.

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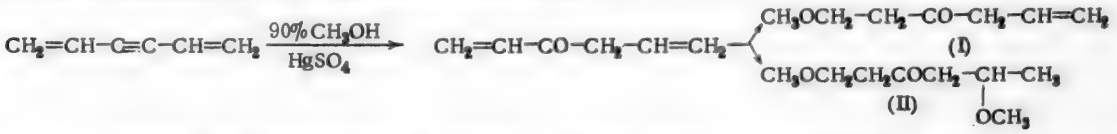
DERIVATIVES OF ACETYLENE. 146. HETEROCYCLIC COMPOUNDS

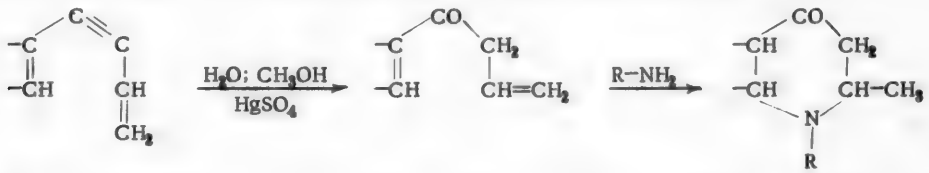
XXII. REACTION OF PRIMARY AMINES WITH 1,5-DIMETHOXYHEXANE-3-ONE AND WITH 7-METHOXY-5-ISOBUTYL-1,5-HEPTADIENE-4-ONE

I. N. Nazarov and S. A. Vartanyan

It has been shown in the preceding reports [1,2] that divinylacetylene, when heated with aqueous methanol in the presence of mercury sulfate, hydrates smoothly with the formation of vinylallyl ketone which, under the conditions of the experiment, will add one or two molecules of methanol, giving a mixture of methoxy ketones (I and II), with a predominance of 1,5-dimethoxyhexan-3-one (II):



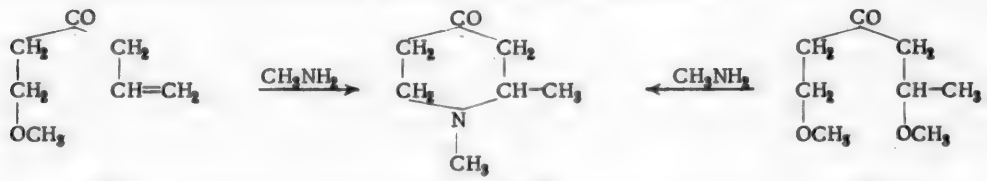
Recently there was worked out, in the authors' laboratory, a new simple method for the synthesis of γ-piperidones [3], by way of interaction of ammonia and primary amines with vinylallyl ketones which are easily obtained by the hydration of divinylacetylenic hydrocarbons in aqueous methanol:



These simple reactions connect acetylene with the diverse compounds of the piperidinic series, to which belong many important, naturally-occurring alkaloids, giving a wide range of possibilities for the syntheses of new physiologically-active substances, in particular, those of analgesic and anesthetic actions.

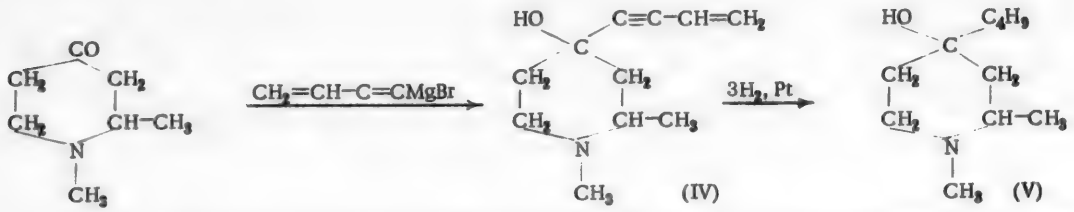
For the purpose of further working out these important reactions, the authors investigated the reaction of primary amines with vinylallyl ketone and its corresponding methoxy ketones (I and II), obtained by hydration of divinylacetylene.

Upon reaction of an aqueous solution of methylamine acetate with methoxyketones (I and II), there was obtained, in 60% yield, the above-described [3] 1,2-dimethyl-4-piperidone (III):

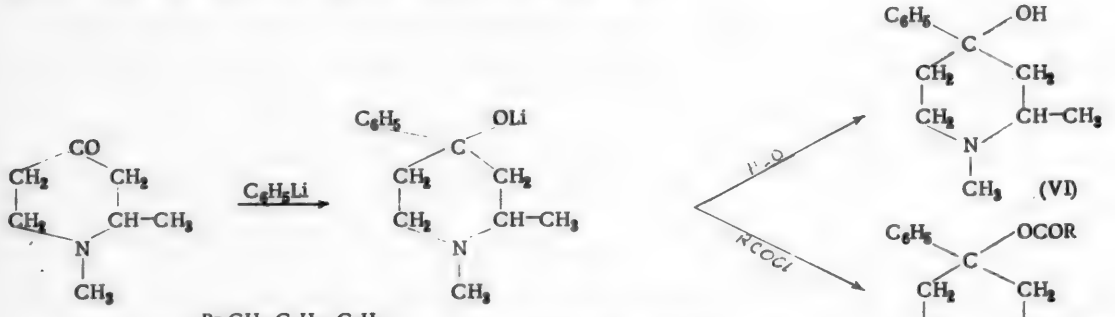


Unlike other γ-piperidones, 1,2-dimethyl-4-piperidone is completely unable to enter into condensation with acetylene and vinylacetylene in the presence of pulverized potassium hydroxide, because it so quickly solidifies into a hard insoluble product [4]. However, the reaction of magnesiumbromovinylacetylene [5] with 1,2-dimethyl-4-piperidone proceeds normally and leads to the formation of 1,2-dimethyl-4-vinylethenyl-4-

piperidol (IV) which, upon hydrogenation with Pt catalyst, absorbs 3 molecules of hydrogen and converts into 1,2-dimethyl-4-butyl-4-piperidol (V):

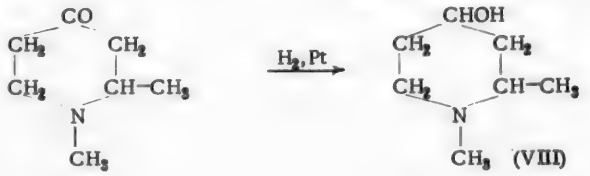


Upon reaction of lithiumphenyl [6] with 1,2-dimethyl-4-piperidone, there is obtained the lithium alcoholate of the tertiary alcohol, which, upon decomposition with water, yields 1,2-dimethyl-4-phenyl-4-piperidol (VI), and by reaction with acid anhydrides, forms the corresponding esters (VII):

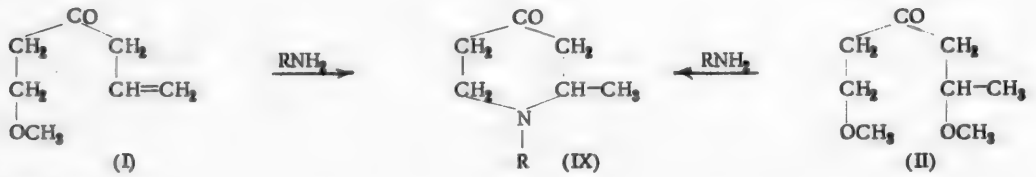


R= CH_3, C_2H_5, C_6H_5.

Upon reduction of 1,2-dimethyl-4-piperidone in alcohol solution, in the presence of Pt catalyst, there is absorbed one molecule of hydrogen to form, 1,2-dimethyl-4-piperidol (VIII):

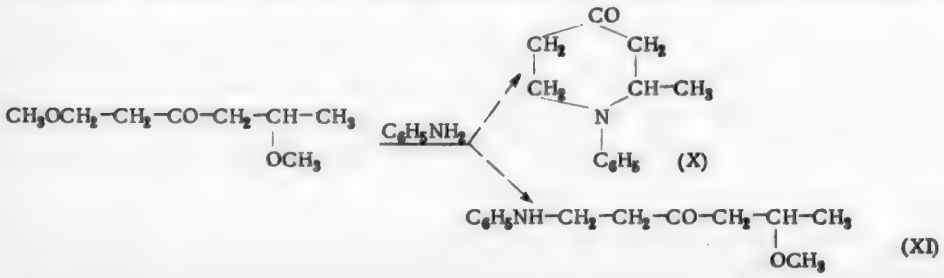


Reactions of the methoxy ketones (I and II) with higher primary amines (ethyl-amine, propylamine) proceed analogously, forming corresponding γ-piperidones (IX) with yields up to 30%.



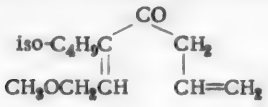
R = C_2H_5, C_3H_7

In the indicated manner, it is easy not only to obtain a variety of 1-alkyl-2-methyl-4-piperidones (IX), but also compounds containing nitrogen aromatic radicals. Thus, for example, upon reaction of aniline with 1,5-dimethoxyhexane-3-one there is obtained 1-phenyl-2-methyl-4-piperidone (X), whereas, at the same time, under milder conditions of reaction, there apparently forms 5-methoxy-1-phenylaminohexan-3-one (XI):

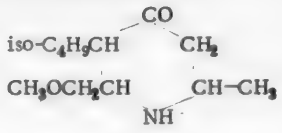


In one of the preceding articles [7] the authors described the obtaining of dienone (XII), which, upon reaction with ammonia, easily formed piperidone (XIII), containing a methoxyl group in the side chain.

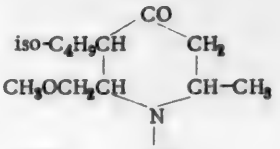
Upon reaction of methylamine with 7-methoxy-5-isobutyl-1,5-heptadiene-4-one (XII) there is obtained in good yield 1,2-dimethyl-5-isobutyl-6-methoxymethyl-4-piperidone (XIV):



(XII)



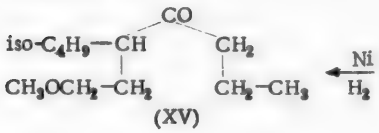
(XIII)



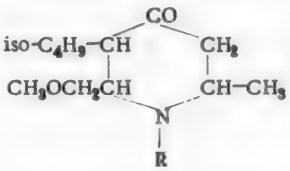
(XIV)

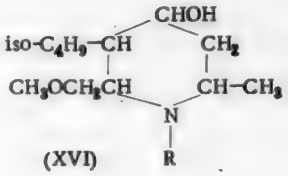
Piperidones (XIII) and (XIV), in contrast to γ-piperidones (not containing the methoxyl group) are completely incapable of condensing with acetylene in the presence of powdered potassium hydroxide [8], and also in liquid ammonia. Condensation does not take place between piperidone (XIV) and lithium phenyl when the reaction mass is heated for three hours at the boiling temperature of ether.

Upon catalytic hydrogenation in an autoclave at 120 atm. and 150° in the presence of Ni catalyst, piperidones (XIII and XIV) split, with the formation of a saturated ketone and ammonia or methylamine. However, upon reduction of piperidone (XII) with sodium in alcohol, there was obtained in high yield the corresponding secondary piperidol (XVI, R = H):



(XV)





(XVI)

R = H and CH_3.

EXPERIMENTAL

The methoxy ketones (I and II) used in the experiments were prepared as described previously [1,2] by hydration of divinylacetylene in aqueous methanol in the presence of mercury sulfate. Because, upon reaction of ammonia and primary amines with methoxy ketones (I and II) there are obtained one and same products, it is therefore more expedient to react the mixture of these methoxy ketones without subjecting them to previous fractional distillation.

1,2-Dimethyl-4-piperidone (III). A 30 g mixture of methoxyketones (I and II) (b.p. 83-87° at 9 mm; n_D^{20} 1.4300), 30 ml of glacial acetic acid, 30 g of 30% aqueous solution of methylamine and 10 ml of dioxane was vigorously mixed by an automatic stirrer at 60° for 5.5 hours. The solution was neutralized with 20% hydrochloric acid to a weak acid reaction, and the neutral products extracted with ether. The organic bases were salted out with potash, extracted with ether, dried with sodium sulfate and distilled in vacuo. 13 g of the earlier described [3] 1,2-dimethyl-4-piperidone (III) was obtained in the form of a mobile liquid, turning yellow on standing, with a characteristic amine odor, b.p. 80-83° at 10 mm; n_D^{20} 1.4583. From the neutral products there was obtained 3.1 g of the original ketones (b.p. 76-79° at 6 mm; n_D^{20} 1.4291).

Reduction of 1,2-dimethyl-4-piperidone. 4.7 g of freshly distilled 1,2-dimethyl-4-piperidone was hydrogenated in 15 ml of ethanol with Pt catalyst. 800 ml of hydrogen was absorbed. For reduction of the carbonyl group to the alcoholic group 800 ml of hydrogen is required. Hydrogenation was complete after 6 hours. As the result of fractional distillation there was obtained 3.9 g of 1,2-dimethyl-4-piperidol (VIII) in the form of a transparent mobile liquid with a faint amine odor; b.p. 78-80° at 3 mm.

n_D^{20} 1.4750; d_4^{20} 0.9554; MR_D 38.10; calculated 37.91.

The hydrochloride of this alcohol is represented as a white powder, m.p. 185-187°.

1.970 mg substance: 0.592 ml 0.02 N $AgNO_3$. 3.438 mg substance: 1.045 ml 0.02 N $AgNO_3$.
Found %: Cl 21.30; 21.55. $C_7H_{15}N \cdot HCl$. Calculated %: Cl 21.45.

1,2-Dimethyl-4-phenyl-4-piperidol (VI). In a round-bottomed flas, equipped with mechanical stirrer, dropping funnel and reflux condenser, was prepared a solution of phenyllithium in a nitrogen atmosphere from

1 g of small fragments of lithium and 13 g of bromobenzene in 50 ml of absolute ether. To the phenyllithium obtained in this manner was added dropwise, during 1.5 hours at 0° temperature, 7.3 g of 1,2-dimethyl-4-piperidone, dissolved in an equal volume of ether. Stirring was continued for two more hours at room temperature and 1.5 hours at boiling temperature of ether. The product was hydrolyzed with 10 ml of water, and after careful shaking in a separatory funnel the aqueous layer was separated, saturated with potash and extracted with ether. The ether extractions were combined, dried by sodium sulfate, and after driving off the ether, the product was fractionally distilled in vacuo. Obtained was 4.3 g of 1,2-dimethyl-4-phenyl-4-piperidol (IV) with a b.p. of 129-131° at 2.5 mm, which crystallized upon dilution with ether, and melted at 123-124° (from light benzene).

12.25 mg substance: 34.31 mg CO_2; 10.47 mg H_2O. 9.13 mg substance: 25.59 mg CO_2; 7.86 mg H_2O. Found %: C 76.45, 76.50; H 9.54, 9.64. $C_{13}H_{19}ON$. Calculated %: C 76.09; H 9.21.

1,2-Dimethyl-4-phenyl-4-piperidol is readily soluble in acetone, alcohol and benzene, poorly so in water; its hydrochloride upon standing in air liquifies.

The acetate of 1,2-dimethyl-4-phenyl-4-piperidol (VII, R = CH_3). In a three-necked round-bottomed flask, equipped with mecanical stirrer and mercury seal, a dropping funnel, a tube for introducing nitrogen (the whole reaction being conducted in nitrogen atmosphere), and a thermometer, there were placed 50 ml of absolute ether and 1.1 g of small lithium fragments. To this mixture was added 2 g of bromobenzene and, reaction started, 10 more g of bromobenzene was gradually added, dissolved in 10 ml of ether. The reaction mixture was then heated for 1.5 hours at the temperature of boiling ether. To the phenyllithium prepared in this manner, was added 9 g of 1,2-dimethyl-4-piperidone, in an equal volume of ether, at -15° for 1 hour. After addition of the piperidone, mixing was continued for 1.5 hours at -15°, 2 hours at room temperature, and 1.5 hours at the temperature of boiling ether. To the reaction mixture was added 30 ml of ether, the mixture was cooled to minus 10°, and then 7 g of acetyl chloride in 15 ml of dry ether was added dropwise during 1 hour. On the following day, the reaction mass was heated at the temperature of boiling ether for 1.5 hours. The product was hydrolyzed with 10 ml of water, salted out with potash, extracted four times with ether, dried with magnesium sulfate and distilled in vacuo. 2.1 g of 1,2-dimethyl-4-phenylpiperidol acetate was obtained (VII, R = CH_3) in the form of a yellowish liquid with ammoniacal odor; b.p. 123-125° at 2 mm; n_D^{20} 1.5171; d_4^{20} 1.0510; MR_D 70.93; calculated 71.13).

Upon mixing this acetate with a saturated alcoholic solution of picric acid, the picrate was obtained in the form of a brown powder, m.p. 157-158° from alcohol.

3.298 mg substance: 0.363 ml N_2 (26°, 738 mm). 3.048 mg substance: 0.335 ml N_2 (26°, 737 mm). Found %: N 12.20, 12.17. $C_{21}H_{24}O_9N_4$. Calculated %: N 11.76.

Upon recovery the hydrochloride of the acetate liquefies in absolute ether and precipitates out in the form of a non-crystallizable oil.

Propionate of 1,2-dimethyl-4-phenyl-4-piperidol. (VII, R = C_2H_5). To the phenyllithium, prepared, as described above, from 2.2 g of metallic lithium and 25 g of brombenzene in a solution of 50 ml of absolute ether, was added dropwise at a temperature of -10° over a period of 1 hour, 15 g of 1,2-dimethyl-4-piperidone in an equal volume of absolute ether. On the following day the reaction mixture was again stirred for 3 hours at the temperature of boiling ether, and to the mixture was added dropwise 30 g of propionic acid anhydride. Stirring was then continued for 1 hour at room temperature and 3 hours at the temperature of boiling ether. The product was treated with water (30 ml), salted out with potash, extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo. 5.5 g of the propionate of 1,2-dimethyl-4-phenyl-4-piperidol was obtained (VII, R = C_2H_5) in the form of a yellow liquid, darkening upon standing; b.p. 128-130° at 2 mm.

n_D^{20} 1.5165; d_4^{20} 1.0400; MR_D 75.90; calculated 75.74.

13.02 mg substance: 35.14 mg CO_2; 10.45 mg H_2O. 13.35 mg substance: 35.88 mg CO_2; 10.60 mg H_2O. Found %: C 73.66, 73.35; H 8.91, 8.85. $C_{16}H_{23}O_2N$. Calculated %: C 73.56; H 8.81.

Picrate – Light yellow, fine crystals, with an m.p. of 150-151° from alcohol.

Tartrate. 0.3 g of the propionate was dissolved in 5 ml of dry acetone and a solution of 0.2 g of tartaric acid in 3 ml of acetone was added. After removal of the acetone, there remained a thick mass, which, upon washing with ether, became hard and brittle; softening point 100-108°. Upon attempting to recrystallize from other solvents, the product separated in the form of an oil.

Benzoate of 1,2-dimethyl-4-phenyl-4-piperidol (VII, R = C_6H_5). To the phenyllithium, prepared, as described above, from 1.2 g of small lithium fragments and 15.4 g of bromobenzene in 50 ml of absolute ether, 10 g of 1,2-dimethyl-4-piperidone in an equal volume of ether was added dropwise at a temperature of -10°. After the addition of piperidol, mixing was continued for 2 hours at a temperature of -10°, 4 hours at room temperature and 2 hours at the temperature of boiling ether. After dilution of the reaction mixture with 50 ml of ether, the mixture was cooled to -12°, and to it added, dropwise, with stirring, 20 ml of benzoyl chloride in a solution of 30 ml of ether. Stirring was continued an additional 2 hours at room temperature and the reaction mixture left for the night. On the following day, the mixture was stirred for 2 hours at the temperature of boiling ether. The product was hydrolyzed with water (20 ml), salted out with potash, extracted three times with ether, dried with sodium sulfate and fractionally distilled in vacuo. 3.2 g of the benzoate of 1,2-dimethyl-4-phenyl-4-piperidol (VII, R = C_6H_5) was obtained in the form of a very viscous oil, b.p. 144-148° at 2 mm. Upon standing, there precipitated from this oil crystals, m.p. 155-156° (from carbon tetrachloride).

6.452 mg substance: 0.284 ml N_2 (26°, 738 mm). 5.308 mg substance: 0.225 ml N_2 (24°, 739 mm). Found %: N 4.72, 4.88. $C_{20}H_{23}O_2N$. Calculated %: N 4.53.

1,2-Dimethyl-4-vinylethyl-4-piperidol (IV). In a round-bottomed flask, equipped with mechanical stirrer, dropping funnel and reflux condenser, ethylmagnesium bromide was prepared from 10 g of magnesium and 50 g of ethyl bromide in a solution of 70 ml absolute ether. Into the ether solution of ethylmagnesium bromide, with cooling by cold water, there was passed, for 1 hour, 30 g of vinylacetylene. The reaction mass was stirred for 2 hours at room temperature, and 1 hour at the boiling temperature of ether, to complete the evolution of ethane. To the magnesiumbromovinyl acetylene obtained in this manner, there was added over a period of 3 hours at a temperature of -10°, 15 g of 1,2-dimethyl-4-piperidone, dissolved in an equal volume of ether, and the reaction mixture was left for the night. On the following day, the product was hydrolyzed with 18% hydrochloric acid (15 ml) at a temperature of -10°, the aqueous layer of the base was salted out with potash, extracted five times with ether and dried with sodium sulfate. As a result of fractional distillation of the product in vacuo, there was obtained 5.3 g of vinylacetylenepiperidol (IV), which appeared in the form of a viscous liquid with a base odor, b.p. 100-102° at 3 mm.

6.962 mg substance: 0.461 ml N_2 (23°, 743 mm). 6.669 mg substance: 0.432 ml N_2 (23°, 743 mm). Found %: N 7.47, 7.31. $C_{11}H_{17}ON$. Calculated %: N 7.82.

The hydrochloride of this alcohol precipitated in the form of a viscous, non-crystallizable mass.

Hydrogenation of 1,2-dimethyl-4-vinylethyl-4-piperidol. 2.7 g of freshly distilled vinylacetylenepiperidol (IV) in a solution of 18 ml of ethanol was hydrogenated in the presence of Pd catalyst. In 1 hour, 1 liter of hydrogen was absorbed, and 72 ml more was absorbed slowly. For the full hydrogenation of one triple, or of two double, bond(s) is required 1.08 liters of hydrogen. As a result of fractional distillation of the hydrogenated product, there was obtained 2.17 g of butylpiperidol (V), in the form of a clear, viscous liquid, with a characteristic base smell; b.p. 96-97° at 3 mm.

11.30 mg substance: 29.30 mg CO_2; 12.54 mg H_2O. 9.27 mg substance: 23.94 mg CO_2; 10.47 mg H_2O. Found %: C 70.76, 70.48; H 12.42, 12.64. $C_{11}H_{23}ON$. Calculated %: C 71.35; H 12.40.

1-Phenylamino-5-methoxyhexan-3-one (XI). A mixture of 10 g of 1,5-dimethoxyhexan-3-one (II), 10 g of freshly distilled aniline, 5 ml of water and 15 ml of dioxane was heated in a flas at 100° for 10 hours. The solution was neutralized with dilute hydrochloric acid to a weak acid reaction, and, after extraction of the neutral products, the organic bases were salted out with potash, extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo. Obtained was 6.1 g of methoxyketamine (XI), b.p. 138-140° at 2.5 mm.

n_D^{20} 1.5315; d_4^{20} 1.0820; MR_D 63.41; calculated 63.86.

7.770 mg substance: 0.456 ml N_2 (23°, 746 mm). 7.780 mg substance: 0.437 ml N_2 (23°, 746 mm). Found %: N 6.36, 6.64. $C_{13}H_{19}O_2N$. Calculated %: N 6.33.

From the ether extraction of neutral products was recovered 2.3 g of 1,5-dimethoxyhexan-3-one.

1-Phenyl-2-methyl-4-piperidone (X). A mixture of 10 g of methoxyketones (I and II) (b.p. 83-87° at 9 mm; n_D^{20} 1.4300), 10 g of freshly-distilled aniline, 5 ml of water and 18 ml of dioxane was heated in a flask at 123-130° for 8 hours. The solution was neutralized with dilute hydrochloric acid to a weak acid reaction, and the neutral products were extracted with ether. The organic bases were salted out with potash, extracted with ether,

dried with sodium sulfate and fractionally distilled in vacuo. Obtained was 4.3 g of 1-phenyl-2-methyl-4-piperidone (X) in the form of a viscous liquid, turning yellow on standing, with an amine odor; b.p. 118-120° at 3 mm.

n_D^{20} 1.5500; d_4^{20} 1.0704; MR_D 56.30; calculated 55.78.

7.710 mg substance: 0.529 ml N_2 (23°, 740 mm). 6.679 mg substance: 0.445 ml N_2 (23°, 740 mm) Found %: N 7.49, 7.70. $C_{12}H_{15}ON$. Calculated %: N 7.41.

From the ether solution of neutral products was recovered 1.2 g of 1,5-dimethoxyhexan-3-one.

1-Propyl-2-methyl-4-piperidone (IX, R = C_3H_7). A mixture of 10 g of methoxyketones (I and II) (b.p. 83-87° at 9 mm n_D^{20} 1.4300), and 10 g of 40% aqueous solution of propylamine was mixed with water cooling (heating up was noticed), and heated on a water bath further at 60° for 1.5 hours, and then treated as in the preceeding experiment. Obtained was 2.3 g of 1-propyl-2-methyl-4-piperidone (IX, R = C_3H_7), in the form of a mobile liquid with an amine odor; b.p. 72-74° at 3 mm.

n_D^{20} 1.4615; d_4^{20} 0.9521; MR_D 44.78; calculated 45.51.

1.569 mg substance: 0.130 ml N_2 (22°, 740 mm). Found %: N 9.30. $C_9H_{17}ON$. Calculated %: N 9.03.

1-Ethyl-2-methyl-4-piperidone (IX, R = C_2H_5). A mixture of 12 g of methoxyketones (I and II) (b.p. 83-87° at 9 mm; n_D^{20} 1.4300), 12 ml of water, 4.5 g of ethylamine and 10 ml of glacial acetic acid was stirred with a mechanical stirrer at a temperature of 60° for 3 hours. The solution was neutralized with 20% hydrochloric acid to a weak acid solution and the neutral products extracted with ether. The organic bases were salted out with potash, extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo. Obtained was 3.4 g of 1-ethyl-2-methyl-4-piperidone (IX, R = C_2H_5), in the form of a mobile liquid, turning yellow upon standing, with a characteristic amine odor; b.p. 67-68° at 3 mm.

n_D^{20} 1.4590; d_4^{20} 0.9420; MR_D 40.9; calculated 40.89.

7.25 mg substance: 1.03 ml 0.05 N $KH(IO_3)_2$. 9.45 mg substance: 1.33 ml 0.05 N $KH(IO_3)_2$. Found %: N 9.92, 9.83. $C_8H_{15}ON$. Calculated %: N 9.93.

The picrate of 1-ethyl-2-methyl-4-piperidone melted at 149-150°.

1,2-Dimethyl-5-isobutyl-6-methoxymethyl-4-piperidone (XIV). A mixture of 28 g of 5-isobutyl-7-methoxy-1,5-heptadiene-4-one (XII) (b.p. 95-97° at 5 mm; n_D^{20} 1.4700) [7] and 35 g of 35% methylamine was heated in a metal flask at 60° for 2 hours. The excess methylamine was driven off on a water bath at 45° in vacuo 70 mm. The solution was neutralized with hydrochloric acid to a weak acid reaction, and the neutral products extracted with ether. The organic bases were salted out by potash, extracted with ether and dried with sodium sulfate, followed by fractional distillation in vacuo. Obtained was 25 g of the piperidone (XIV) in the form of a viscous liquid, turning yellow on standing, with a characteristic amine odor; b.p. 117-119° at 2 mm.

n_D^{20} 1.4750; d_4^{20} 0.9702; MR_D 65.85; calculated 65.62.

10.36 mg substance: 25.96 mg CO_2; 10.04 mg H_2O. 10.28 mg substance: 25.82 mg CO_2; 9.83 mg H_2O. Found %: C 68.38, 68.55; H 10.84, 10.70. $C_{13}H_{25}O_2N$. Calculated %: C 68.72. H 11.01.

The picrate precipitated in the form of a dark, non-crystallizable mass. The hydrochloride was completely unstable, and immediately liquified. From the neutral products of the ether solution was recovered 3.7 g of original ketone (XII) (b.p. 94-98° at 6 mm; n_D^{20} 1.4700).

Hydrogenation of 1,2-dimethyl-5-isobutyl-6-methoxymethyl-4-piperidone. 10 g of freshly distilled piperidone (XIV), b.p. 117-119° at 2 mm; n_D^{20} 1.4750 in 25 ml of ethanol was hydrogenated in the presence of Raney nickel catalyst in an autoclave at a hydrogen pressure of 120 atmospheres and a temperture of 150°. During 4 hours the pressure fell to 8.5 at 150°, in the autoclave. The reduction product, with a strong odor of methylamine, was filtered off from the catalyst and fractionally distilled in vacuo. Upon distillation the following fractions were obtained (at 5 mm): first fraction, b.p. 93-100°; n_D^{20} 1.4373 - 2.7 g; 2 fraction, b.p. 100-127°; n_D^{20} 1.4640 - 0.9 g; 3rd fraction, b.p. 127-132°; n_D^{20} 1.4720 - 5.2 g; resinous sediment 0.8 g.

Upon repeated fractional distillation of the first fraction there was separated the earlier-described 7-methoxy-5-isobutylheptan-4-one (XV) with a b.p. of 118-120° at 18 mm; n_D^{20} 1.4345 [7].

In a similar manner goes the hydrogenation of 2-methyl-5-isobutyl-6-methoxymethyl-4-piperidone (XIII). At a pressure of 85 atmospheres and a temperature of 100°, the piperidone ring is split, and under milder conditions the product does not hydrogenate.

2-Methyl-5-isobutyl-6-methoxymethyl-4-piperidol (XVI, R=H). 16 g of piperidone (XIII) (b.p. 110-112° at 6 mm; n_D^{20} 1.4700) was dissolved in 350 ml of alcohol and 35 g of metallic sodium in small pieces was added slowly. When the sodium was completely dissolved, to the mixture was then added, dropwise, while cooling with ice water, 160 ml of concentrated hydrochloric acid to an acid reaction. The product was filtered off from the sodium chloride, the precipitate washed three times with alcohol and water, and the water-alcohol solution of the hydrochloride was evaporated off in vacuo to a volume of 40 ml. The remaining viscous oil was neutralized with soda, salted out with potash, extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo. Obtained was 13.6 g of 2-methyl-5-isobutyl-6-methoxymethyl-4-piperidol (XVI, R=H) in the form of a viscous liquid with amine-like odor; b.p. 118-119.5° at 4 mm.

11.66 mg substance: 28.39 mg CO_2; 12.33 mg H_2O. 12.66 mg substance: 30.74 mg CO_2; 13.17 mg H_2O. Found %: C 66.45, 66.32; H 11.84, 11.65. $C_{12}H_{25}O_2N$. Calculated %: C 66.96; H 11.62.

SUMMARY

During the interaction of primary amines with vinylallylketone, or with its corresponding methoxyketones (I and II), obtained by hydration of divinylacetylene in aqueous methanol, there are formed N-substituted 2-methyl-4-piperidones (IX, R=CH_3, C_2H_5, C_3H_7, C_6H_5). Obtained also are 1,2-dimethyl-4-piperidol (VIII), 1,2-dimethyl-4-vinylethenyl-4-piperidol (IV), 1,2-dimethyl-4-butyl-4-piperidol (V), 1,2-dimethyl-4-phenyl-4-piperidol (VI), its esters (VII; R=CH_3, C_2H_5, C_6H_5), 1,2-dimethyl-5-isobutyl-6-methoxymethyl-4-piperidone (XIV) and 2-methyl-6-isobutyl-6-methoxymethyl-4-pipetidol (XVI).

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N-ARYLAMIDES OF HYDROXYCARBOXYLIC ACIDS AND THEIR CONVERSION INTO HETEROCYCLIC COMPOUNDS

XVIII. RELATION BETWEEN SAPONIFICATION OF ARYLAMIDES OF α-, β-, AND γ-HYDROXYCARBOXYLIC ACIDS AND THE EASE OF HETEROCYLIC RING CLOSURE

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The saponification of arylamides of α-, β-, and γ-hydroxycarboxylic acids was conducted in both acid and in alkaline medium. The percentage of arylamide saponified was determined by the amount of aromatic amine obtained as a result of the reaction. The latter was determined by the sodium nitrite titration method utilized by B. A. Porai-Koshits and coworkers [1], in the study of azomethine hydrolysis reactions. Saponification in alkaline medium was carried out in the following manner. In a flask equipped with a reflux condenser there was placed an accurately-weighed portion of arylamide, 45-60 moles of 10% KOH solution was poured in, and the mixture boiled for one hour. The aromatic amine was quantitatively determined as indicated above. The data obtained are shown in Table 1.

TABLE 1

No.	Formula of anilide	Weight of substance (in g)	0.05 N $NaNO_2$ (in ml)	Saponified arylamide (in %)
1	$C_6H_5NHCOC(OH)(CH_3)_2$	0.0928	5.24	50.54
2	$C_6H_5NHCOC(OH)(C_2H_5)_2$	0.0827	0.35	4.38
3	$C_6H_5NHCOC(OH)(C_5H_{11}\text{-iso})_2$	0.1009	0.4	5.77
4	$p\text{-}CH_3C_6H_4NHCOC(OH)(C_6H_4CH_3\text{-}o)_2$	0.1485	Does not saponify	
5	$C_6H_5NHCOCH_2C(OH)(C_6H_5)_2$	0.1268	0.91	11.33
6	$C_6H_5NHCO(CH_2)_2C(OH)(CH_3)_2$	0.1230	8.6	72.3
7	$C_6H_5NHCO(CH_2)_2C(OH)(CH_2CH=CH_2)_2$	0.1339	7.56	73.1
8	$C_6H_5NHCO(CH_2)_2C(OH)(C_6H_4OCH_3\text{-}o)_2$	0.1950	7.8	78.2

The p-toluidide of o-tolyl acid upon boiling for one hour with 50% KOH solution was only 7.23% saponified, and with 0.5 N alcoholic KOH solution for 1 hr., only 10.3%. The exceptional resistance to hydrolysis of benzylanilide was observed by McKenzu and Duff [2]. Upon boiling with concentrated alkali solution, and even upon melting with solid alkali, the authors [2] did not obtain satisfactory results.

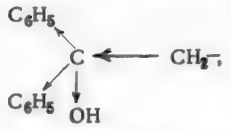
Saponification in acid medium was carried out with the aid of 10% HCl solution. Boiling lasted 1 hour. 50 to 70 moles of acid was taken, depending upon the weight of arylamide taken. The saponification data are given in Table 2.

Upon boiling the p-toluidide of o-tolyl acid with 25% HCl solution, it was only saponified to the extent of 4.83%. Upon lengthy boiling of the p-bromanilide of benzilic acid with 50% H_2SO_4 solution, there was separated a very small amount of 4-bromaniline. It is possible to assume that the reaction goes in the direction of intramolecular condensation with the formation of oxindole derivatives. An experiment performed with the p-phenetidine of benzilic acid and 50% H_2SO_4 solution did not confirm this assumption. Thus the data cited in literature reference [3], referring to the intramolecular condensation of N-ethylbenzilanilide with the aid of 50% H_2SO_4 solution, become doubtful. More concentrated solutions of the acid are not recommended for saponification, in order to avoid possible intramolecular condensation. The mechanics of saponification of esters, and of carboxylic acid amides, are sufficiently explained [4] and the authors do not consider it worth while to dwell upon this question. The difficulty in saponifying the arylamides of benzilic, o-tolyl and diisoamylglycol acids, both in acid and in alkaline medium, should be explained by manifestation of a steric effect, conditioned by the presence at the α-carbon atom of an aromatic and a branched aliphatic radical. The anilide of β,β-diphenyl-β-hydroxypropionic acid (Experiment 5, Tables 1 and 2) saponifies better, because, with the removal of the tertiary alcohol group from the chain, the steric effect is diminished, and the electrochemical effect of the radical begins to appear.

TABLE 2

No.	Formula of anilide	Weight of substance (in g)	0.05 N $NaNO_2$ solution (in ml)	Saponified arylamide (in %)
1	$C_6H_5NHCOC(OH)(CH_3)_2$	0.1000	5.44	48.69
2	$C_6H_5NHCOC(OH)(C_2H_5)_2$	0.1024	3.1	31.33
3	$C_6H_5NHCOC(OH)(C_5H_{11}\text{-iso})_2$	0.1113	0.5	6.54
4	$p\text{-}CH_3C_6H_4NHCOC(OH)(C_6H_4CH_3\text{-}o)_2$	0.1293	Does not saponify	
5	$C_6H_5NHCOCH_2C(OH)(C_6H_5)_2$	0.1389	0.3	3.42
6	$C_6H_5NHCO(CH_2)_2C(OH)(CH_3)_2$	0.1426	12.29	89.26
7	$C_6H_5NHCO(CH_2)_2C(OH)(CH_2CH=CH_2)_2$	0.1109	8.56	99.99
8	$C_6H_5NHCO(CH_2)_2C(OH)(C_6H_4OCH_3\text{-}o)_2$	0.2315	8.6	72.6

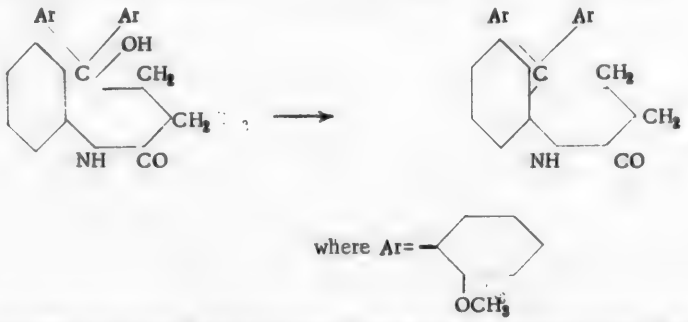
Adjacent to the carbonyl carbon atom of the anilide of β,β-diphenyl-β-hydroxypropionic acid are three groups ($2C_6H_5$– and OH),



possessing –I-effects, and only one group (CH_2) a +I-effect. On the whole, the indicated grouping will attract electrons, according to the mechanism of inductive replacement. This anilide saponifies more readily in alkaline medium because, in accordance with the mechanism of the reaction, the saponification in alkaline medium is speeded up by the presence of the group possessing a minus I-effect.

Arylamides of γ-hydroxycarboxylic acids saponify easily both in acid and in alkaline medium. In the case of radicals with a tertiary alcoholic group, in aryl amides of γ-hydroxycarboxylic acid, an impediment is no longer formed, and the nature of the radicals is of little effect because, with recession over the chain, the force of the inductive effect diminishes to a considerable degree [4]. It was of interest to clarify the relation between ease of saponification of arylamides of hydroxycarboxylic acids and their ability to close the ring. The authors determined [5] that those arylamides condense, which with concentrated sulfuric acid, give a carbonium ion with an electron deficiency on the central carbon atom. From this point of view the authors were interested in those arylamides which have two aromatic radicals at the carbinol carbon atom.

Comparing data obtained by the authors on the saponification of the arylamides of α-, β-, and γ-hydroxycarboxylic acids with their tendency for intramolecular condensation, the following can be noted. Arylamides of α-hydroxycarboxylic acids exhibit selective resistance to saponification both in acid and in alkaline medium; at the same time the heterocylic ring is completed with exceptional ease [6]. Arylamides of β-hydroxycarboxylic acids saponify significantly in alkaline medium and somewhat worse in acid medium. They condense less smoothly [7]. Arylamides of γ-hydroxycarboxylic acids saponify very easily and do not condense. Utilizing the methods worked out by the authors, an attempt was made to close the seven-membered heterocyclic ring in the anilide of γ,γ-bis-2-methoxyphenyl-γ-hydroxybutyric acid according to the following scheme:



To the anilide of γ,γ-bis-2-methoxyphenyl-γ-hydroxybutyric acid was added concentrated sulfuric acid, and the reaction mixture heated on a water bath (80-90°) to full dissolution of the anilide and disappearance of the reddish-violet coloring. Simultaneously the anilide of γ,γ-di-o-methoxydiphenylglycolic acid was completely saponified. Aniline was identified in the form of tribromaniline, m.p. 118° [8], and γ,γ-di-o-methoxydiphenylglycolic acid, after precipitation of sulfuric acid with the aid of $Ba(OH)_2$, and treatment with soda solution, with subsequent evaporation, and crystallization in the form of the sodium salt. The sodium salt dissolved readily in water and with concentrated sulfuric acid gave a red-violet coloration (grouping $Ar_2C(OH)$—).

According to their ease of saponification, arylamides of hydroxycarboxylic acids could be arranged in the

order: $\gamma > \beta > \alpha$. According to their ease of heterocyclic formation, they give the reverse order: $\alpha > \beta > \gamma$ (in the latter the heterocyclic ring does not close). Thus, on the basis of saponification can be foreseen condensation.

SUMMARY

1. The saponification reaction of arylamides of α-, β-, and γ-hydroxycarboxylic acids, both in acid and in alkaline medium, was studied.

2. It was determined that, according to the ease of saponification, the arylamides of the hydroxycarboxylic acids have the order $\gamma > \beta > \alpha$, and according to the ease of heterocyclic ring closure, the reverse order $\alpha > \beta > \gamma$ (the latter not condensing).

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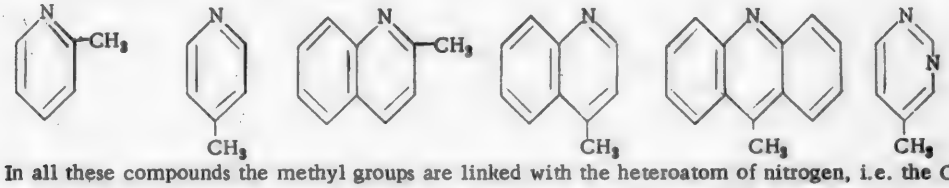
SYNTHESES AND TRANSFORMATIONS OF PYRIMIDINE DERIVATIVES

III. A STUDY OF THE MOBILITY OF HYDROGEN ATOMS OF THE METHYL GROUP IN DERIVATIVES OF MONOHYDROXYDIHYDROPYRIMIDINE

N. V. Khromov-Borisov and A. M. Savchenko

Copious written material pertaining to the study of chemical transformations of pyrimidine compounds, and likewise the results of investigation of derivatives of 4-methyluracil, published by one of the authors with R. S. Karlinskaya [1] demonstrate that the methyl groups arranged on the even positions of the pyrimidine ring possess increased activity. In some cases this activity is so great that the substance appears capable of azo combination reaction at the expense of the hydrogens of the methyl group.

Among the six-membered heterocylic compounds capable of such azo combination are: alkyl halide derivatives of α- and γ-picolines, quinaldine, lepidine and also mesomethylacridine, 5-nitro-4-methyluracil and 5-diazo-4-methyl uracil. It is readily noted that in all these compounds there is a similar arrangement of the methyl group relative to the heteroatoms of nitrogen:



In all these compounds the methyl groups are linked with the heteroatom of nitrogen, i.e. the CH_3 groups are connected to the C=N groups either directly or by the conjugated linkage. This regularity is in complete conformity with electronic concepts concerning the activation mechanism of the CH_3 and CH_2 groups, giving a consistent explanation of the origin of the greater activity of these groups entering into different combinations.

A great number of works from the school of academician A. E. Porai-Koshits has been devoted to the study of the reaction ability of the methyl and methylene groups. These works considerably widened the circle of reactions with active methyl and methylene groups and led to the possibility of a theoretical generalization of accumulated regularities. At the present time the authors are correct in expressing the following rule: if the methyl or methylene group is in conjugation with the heteroatom, [illegible] increased activity acquires to its hydrogen atoms. This rule should be called "The A. E. Porai-Koshits Rule", under which name it has been quoted in the works of his students.*

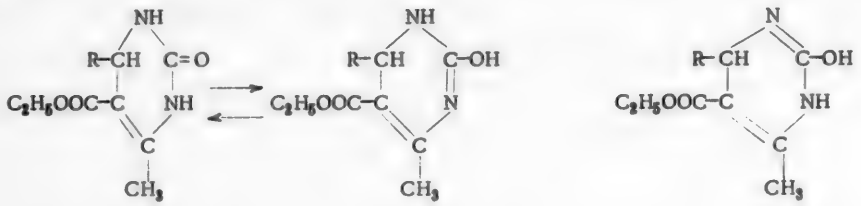
The above-enumerated six-membered heterocyclic compounds possess aromatic character; they contain three double bonds in the ring, upon which the placement of these bonds in the ring is not fixed. If, on the other hand, there could be shown fixation of the double bonds in the molecule of quinaldine or lepidine (after the analogy of naphthalene) then in symmetrical molecules, such as γ-picoline and mesomethylacridine, there would be no substantiation for this hypothesis.

For activation of the methyl group, the presence of three double bonds in the ring is not compulsory from the point of view of the above mechanism. It could even be admitted that in the absence of fixed double bonds in the ring, the binding of a methyl group to the heteroatom to some degree diminishes activation of the methyl group. Up to now, no six-membered heterocyclic compound with two double bonds in the ring and containing an active methyl group has been described. Along this line, we decided to study derivatives of dihydropyrimidine containing the methyl group in position 4.

Fairly easily accessible appear to be the 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidines, containing

* This principle was expressed by N. V. Khromov-Borisov at the meeting of the D. I. Mendeleev All Union Chemical Society on December 6, 1951.

various substitutions in the 6-position. These compounds were obtained for the first time in 1893 by Biginelli [3] by interaction of urea, an aldehyde and acetoacetic ester in absolute alcohol medium and in the presence of concentrated hydrochloric acid. By introducing into the reaction various aldehydes, it was later possible to obtain a whole range of related compounds [4-10]. To them was attributed the following structure (Formula I and II):

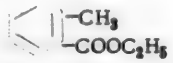


(I) (II) (III)

With such structure the nitrogen heteroatoms cannot activate the methyl group, because the latter is not found in conjugation with them. In addition, the matter is not changed if there is allowed tautomeric displacement of the hydrogen in position 1 (Formula III).

In order to determine whether the above-expressed assumptions are applicable in these cases, the authors decided to study the activity of the methyl groups in two similar compounds (R= H and R= C_6H_5). First of all the authors have established that the compounds studied under sufficiently rigid conditions (melted at 205-210°) are capable of condensing with p-dimethylaminobenzaldehyde. The red products formed are readily soluble in the majority of organic solvents. The condensation product, obtained from 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine (R= H), was purified by repeated reprecipitations from alcohol and reanalyzed. The analysis data confirmed that it is 2-hydroxy-4-(p-dimethylaminostyryl)-5-carbethoxydihydropyrimidine (m.p. 194-198°).

In this manner the methyl groups in the investigated compounds are sufficiently active for condensation reaction with p-dimethylaminobenzaldehyde. Does it not appear to be the consequence of the activation influence of the $COOC_2H_5$ group, being placed in the o-position to the methyl group? But a similar influence is displayed in the known reactions of Claisen and Perkin. To answer this question, the authors proceeded to study the interaction of dihydropyrimidines with diazo compounds. As it is known,

neither $CH_3COOC_2H_5$, nor $CH_3CH=CHCOOC_2H_5$, nor 

are capable of entering into azo combination reaction. The methyl groups in these compounds are under the activating influence of the carbethoxyl group; nevertheless, they do not appear sufficiently active (in the relationship) as regards diazo compounds. Thus it could be anticipated that our dihydropyrimidines will also be incapable of azo combination. Otherwise it would have to be considered that upon the methyl group is somehow transmitted the activating influence of the heteroatoms of the dihydropyrimidine ring.

Substituent in position 6	Diazo compound	M.p. of dye	Color of dye	Color in alkaline medium	Color in acid medium
H	$NO_2-C_6H_4-N=N-OH$	174-176°	Maroon	Blue	Yellow
C_6H_5	Ditto	155-157	Dark-red	Bright-violet	Yellow
H	$NH_2SO_2-C_6H_4-N=N-OH$	Indefinite (above 260°)	Brick-red	Red	Yellow
C_6H_5	Ditto	Indefinite (above 240°)	Brick-red	Raspberry-red	Yellow

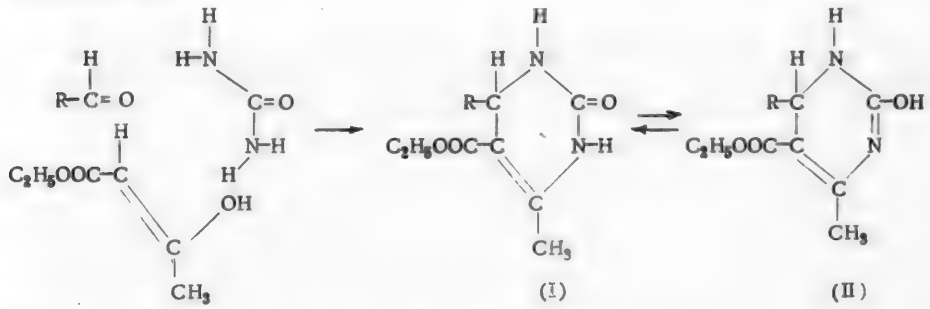
As diazo compounds, the authors took p-nitrodiazobenzene and p-sulfamidodiazobenzene. The reaction was conducted in glacial acetic acid medium, in the presence of anhydrous sodium acetate. It appeared that under these conditions azo combination took place: upon interaction with one mole of the diazo compound,

dyes were obtained, identified as monoazo dyes. The properties of the synthesized azo dyes are cited in the preceding table.

Upon union of the investigated dihydropyrimidines with 2 moles of p-nitrodiazobenzene, there are obtained azo dyes differing in their properties from those quoted in the table. However, they also appear to be monoazo dyes in composition; within the limits of accuracy of the elementary analyses, they do not differ from those quoted in the table. On this basis, it could be assumed that upon reaction of the second molecule of diazo compound there occurs transformation of the dihydropyrimidine nucleus into pyrimidine.

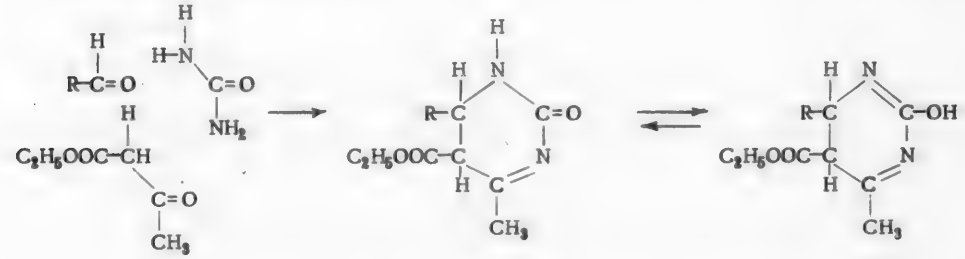
The experimental facts obtained indicate that the methyl group located in the 4-position of the dihydropyrimidines studied possesses great activity, sufficient for interaction with diazo compounds. Further, it will be shown below that this interaction proceeds at the expense of the methyl group. Thus, it should be assumed that the methyl group in these substances is under the activating influence of the dihydropyrimidine ring. However, as we have already seen, the structural formula, suggested by Biginelli for the monohydroxydihydropyrimidines, cannot explain this activating action, inasmuch as the methyl group is not in conjugation with the heteroatoms of the ring.

All these facts and considerations forced the authors to review the question of structure of the investigated dihydropyrimidines. At the time of the structural formula development, Biginelli proceeded from the enol form of acetoacetic ester:



(I) (II)

If it is assumed that acetoacetic ester enters into reaction as the keto form, then the structure of the condensation product will be different:



(III) (IV)

In the compound of such a structure the increased activity of the methyl group becomes understandable, because in it the methyl group is under the activating influence of two groups $>C=N-$. However, it is known that these dihydropyrimidines are capable of combining with two atoms of bromine [11] and this is the argument in favor of Biginelli's structural formula (II). Thus, on the one hand the capability of azo conjugation at the expense of the methyl group necessitates ascribing to these compounds Structure (IV), while on the other hand the capability for bromination necessitates ascribing to them the Structure (II). These facts forced us to assume that the dihydropyrimidines studied represent a mixture of two isomers (II) and (IV).

In addition, the authors were occupied with the experimental verification of their assumption. First of all, it was necessary to determine whether the dibromide has the structure which is ascribed to it. Inasmuch as the investigated compounds contain an active CH_3 group, it was necessary to show that, upon reaction of bromine, there is not substitution of two atoms of hydrogen in the methyl group, but rather linkage of two bromine atoms to the two adjacent carbon atoms. The authors carried out bromination of the investigated dihydropyrimidines (R=H and R=C_6H_5).

Experiment has shown that the obtained dibromides, upon debromination with the aid of zinc dust, transformed into primary dihydropyrimidines. This indicates the presence of two bromine atoms on adjacent carbon atoms. Thus the structure of the dibromides corresponds to the structural Formula (II).

During execution of these experiments it was noticed that the bromination required severe conditions (boiling in chloroform with large excess of bromine) and did not give quantitative yields. This unusual difficulty in bromination cannot be satisfactorily explained by the formula of Biginelli (II), which contains the double bond in position 4-5. Compound (II) should very easily, in the cold, add two atoms of bromine to the double bond C=C, while the compound with structure (IV) should not possess this characteristic. Upon this assumption the authors decided to determine the content percentage of isomer (II) in the dihydropyrimidines studied, by the application of bromometric titration. The determination was conducted in the following manner: to an alcoholic solution of the substance was added in the cold an excess of freshly prepared and titrated alcoholic bromine. The remaining bromine, after addition of potassium iodide, was titrated with hyposulfite, and thus was determined the percentage content of brominated isomer (II).

It was found that at both 0° and 17°, notwithstanding a large excess of bromine (3 moles for 1 mole of substance), bromination proceeds only to a defined limit. This limit is practically obtained within 5 minutes and does not change upon prolonged bromination. Thus the authors determined that 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine contains 6-7% of the brominated isomer, and 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine — 19-21%.

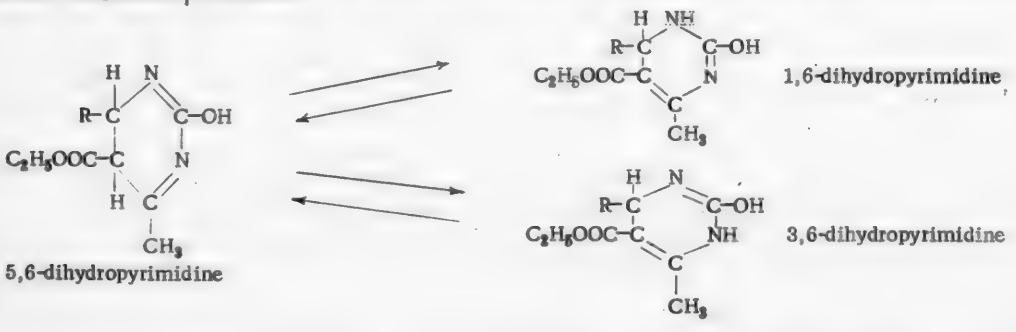
The authors were able to isolate the non-brominable isomers of these dihydropyrimidines in the free state by utilizing the fact that their solubility in aqueous alcohol is smaller than the solubility of the corresponding 4,5-dibromoderivatives. For purification, they were washed many times with water and alcohol; upon attempt to recrystallize from alcohol partial transformation of the non-brominable isomer into the brominable occurs. The isolated isomers do not absorb bromine at all upon reaction with alcoholic bromine.

Upon boiling the non-brominable isomers in alcohol or benzene, their transformation into brominable isomers occurs, which quantity reaches defined limits, corresponding to the above-mentioned percentage contents. These limits are practically obtained within 1 hour. For example, upon boiling the non-brominable isomer of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine in alcohol or benzene, within 10 minutes the contents of brominable isomer reaches 10-11%, after 30 minutes of boiling —16-17%, after 1 hr of boiling —18-21%. Further boiling does not change the ratio of brominable and non-brominable isomers in the mixture. Boiling of the non-brominable isomers in glacial acetic acid results in higher bromometrical analysis results, which is explained by partial acetylation (see below).

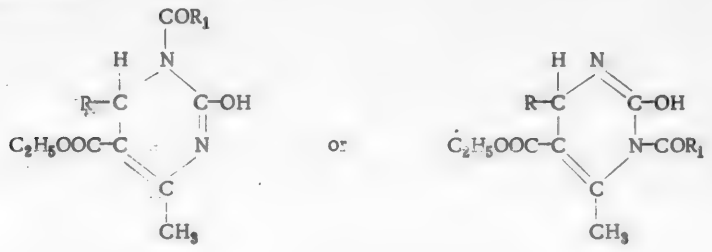
The attainment of one and the same constant limit every time indicates that the observed isomerization of the non-brominable isomer into the brominable represents a reversible process. In boiling alcohol or benzene it proceeds at a measurable rate: the equilibrium point is reached in approximately 1 hr. At 0°, and even at 17°, this rate is so much less that the non-brominable isomers can be successfully separated and can be obtained practically free of the brominable. The reverse process proceeds at a high rate, because in the equilibrium mixture the non-brominable isomers are present in large amount.

The tautomeric transformation consists of migration of the hydrogen atom on carbon 5 to one of the heteroatoms (position 1 or 3), and conversely, with corresponding replacement of the double bonds in the ring.

This tautomerism (desmotropism) explains the ability of the investigated dihydropyrimidines to enter into azo combination reaction at the expense of the hydrogens of the methyl group, and also their ability to add bromine at the double bond. Thus the unusual difficulty of bromination and the necessity for conducting bromination at elevated temperature is clarified.



Examination of the structural formulas of 1,6- or 3,6-dihydropyrimidine derivatives leads to the conclusion that these compounds should be capable of acetylation, similar to dihydrouracil [12], with the formation of 1- or 3-acyl derivatives.

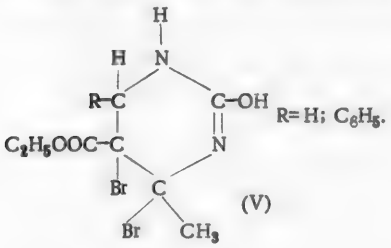


These N-acyl derivatives, no longer being capable of transformation into 5,6-dihydropyrimidine compounds, should easily brominate 100% in the cold, like ethylenic compounds, and at the same time their methyl group should not be reactive.

Experiment fully confirmed these theoretical assumptions. N-acetyl-2-hydroxy-4-methyl-5-carbethoxy-dihydropyrimidine and N-acetyl-2-hydroxy-4-methyl-5-carbethoxy-6-phenyl-dihydropyrimidine, synthesized by the authors, brominated quantitatively under conditions of the above-described bromometrical titration, but did not conjugate with p-nitrodiazobenzene.

Acetylation was effected with acetic anhydride; however, partial acetylation already occurred upon boiling in glacial acetic acid. This explains why boiling the non-brominable tautomers in glacial acetic acid gave above-normal results at the time of bromometric analysis of the produced mixture of tautomers (see above).

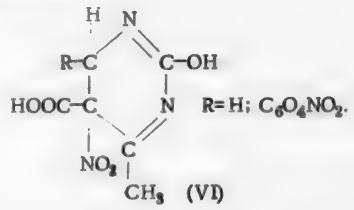
The authors also subjected dibromoderivatives of the investigated dihydropyrimidines to the reaction of diazo combination. The structure of these dibromides is such (V) that displacement of the double bond in position 3-4 is impossible; thus, activation of the methyl group is also impossible. Practice has shown that they are incapable of undergoing azo combination with p-nitrodiazobenzene.



The authors have expressed above an assumption that the investigated dihydropyrimidines enter into azo combination reaction at the expense of the hydrogens of the active methyl group. However, the tautomerism phenomenon detected by the authors points to mobility of the hydrogen atom in position 5. Thus it could be assumed that at the time of azo combination this atom of hydrogen is replaced by the rest of the diazo compound. If such a hypothesis could not emerge from the interaction with p-dimethylamino-benzaldehyde, because two hydrogen atoms situated at one carbon atom are split during this condensation, then during the azo combination reaction such an assumption can develop, since only one hydrogen atom is necessary for monoazo dye formation. In order to eliminate such an assumption, the authors substituted the hydrogen atom in position 5 by a nitro group.

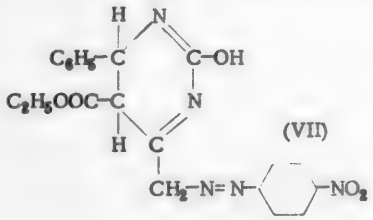
It was found that during reaction of the nitrated mixture with the investigated dihydropyrimidines, there simultaneously occurred nitration and saponification of the carbethoxyl group.

The obtained 2-hydroxy-4-methyl-5-nitrodihydropyrimidine-5-carboxylic acid[(VI), R=H; silky-white needles, m.p. 142.5-143.5°] in pyridine conjugates with p-nitrodiazobenzene. Upon nitration of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine there is formed 2-hydroxy-4-methyl-5-nitro-6-p-nitrophenyldihydropyrimidine-5-carboxylic acid (VI, R=$C_6H_4NO_2$-p). The position of the nitro group in the phenyl radical was determined by means of



oxidation, as the result of which there is formed p-nitrobenzoic acid. The obtained dinitro compound — a white crystalline substance (m.p. 133.5-134.5°) — was soluble in alkali and in carbonates with yellow coloration. Upon acidification of the solution there precipitated a bright-yellow substance of the same composition as the white one, but possessing different properties (decomposed explosively at 117-118°). The authors did not investigate this transformation. Both the white and the yellow substance conjugate in pyridine with p-nitrodiazobenzene. Thus are formed monoazo dyes, similar in their composition, but different in properties. The dye obtained from the white substance, upon solution in alkali and acidification, transforms into the dye obtained from the yellow substance.

The ability of the obtained nitro derivatives to undergo azo combination reaction shows this reaction proceeds at the expense of the methyl group.



(VII)

For final determination of the azo dye structures obtained from dihydropyrimidines, 2-hydroxy-4-nitrobenzeneazomethyl-5-carbethoxy-6-phenyldihydropyrimidine was subjected to the action of bromine in chloroform while heating. The test showed that this dye is unable to take up bromine. Consequently, it could be assumed to represent the 5,6-dihydropyrimidine derivative (VII).

EXPERIMENTAL

Synthesis of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine [3-5]. 6 g of urea, 10.6 g of benzaldehyde, 19.5 g of acetoacetic ester, 40 ml of alcohol and 16 drops of concentrated hydrochloric acid were refluxed for three hours. After cooling, the precipitate was filtered off, washed with alcohol and dried. Yield 23.75 g (84.5% of theoretical). After 4 recrystallizations from alcohol, m.p. 206-207°.

Synthesis of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine [5]. 23.1 g of methyleneurea [13], 53.5 g of acetoacetic ester, 150 ml of glacial acetic acid and 20 drops of concentrated hydrochloric acid were refluxed for 5 hours and then put aside to stand for 14-16 hours. The light yellow precipitate formed was filtered off, washed with a small quantity of aqueous alcohol, and dried. Yield 16.5-18 g (20-22% of theoretical). After a single recrystallization from alcohol the m.p. was 254-256°.

Condensation of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine with p-dimethylaminobenzaldehyde. 1.84 g of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine and 1.49 g of p-dimethylaminobenzaldehyde were melted together for 3 hrs at 205-210°. The cooled cake was extracted with 30 ml of hot alcohol. The refiltered red solution was poured, while mixing, into 10 times its volume of water. The precipitated brick-red solid was purified by dissolution in 30 volumes of alcohol, with subsequent precipitation by an equal volume of water. The substance was soluble in alcohol, acetone, benzene, and chloroform; m.p. 194-198°.

0.0690 g substance: 0.1636 g CO_2; 0.0411 g H_2O. 0.1008 g substance: 0.2382 g CO_2; 0.0574 g H_2O. 0.0908 g substance: 10.5 ml N_2 (24°, 767 mm). 0.1106 g substance: 12.7 ml N_2 (24°, 767 mm). Found %: C 64.66, 64.42; H 6.54, 6.38; N 13.24; 13.16. $C_{20}H_{21}O_3N_3$. Calculated %: C 64.76; H 6.66; N 13.33.

Interaction of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine with 1 mole of p-nitrodiazobenzene. To the cooled solution of 2.6 g of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine and 4 g of anhydrous sodium acetate in 50 ml of glacial acetic acid was added, with mixing, a solution of p-nitrodiazobenzene, prepared from 1.38 g of p-nitraniline, 3.7 ml of concentrated hydrochloric acid, 2.2 ml of water and 0.7 g sodium nitrite dissolved in 2.1 ml of water. The reaction mixture was stirred for 3 hours and put aside for 14-16 hours at room temperature. The filtered solution was diluted with 6 times its volume of water. The precipitated dye weighed 3.1 g (71.4% of the theoretical). For purification, the dye was boiled with water and extracted with 40 ml of ethyl acetate, after evaporation of which there remained a glittering, dark-red sediment. It was 4 times recrystallized from alcohol (40 volumes), which resulted in considerable loss. The purified dye melted with decomposition at 155-157°; with alcoholic alkali a bright violet color resulted. Readily soluble in alcohol, ether, acetone, and acetic acid; less so in benzene and toluene.

0.1033 g substance: 0.2218 g CO_2; 0.0456 g H_2O. 0.1202 g substance: 0.2584 g CO_2; 0.0501 g H_2O. 0.1133 g substance: 17 ml N_2 (22°, 754 mm). 0.1022 g substance: 15.5 ml N_2 (20°, 750 mm). Found %: C 58.58, 58.63; H 4.98, 4.67; N 17.1, 17.3. $C_{20}H_{19}O_5N_5$. Calculated %: C 58.68; H 4.64; N 17.11.

Interaction of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine with 2 moles of p-nitrodiazobenzene. Procedure as in the previous case; there was taken only double the volume of sodium acetate and diazo solution and 60 ml of glacial acetic acid. After 48 hours 2.1 g of the dye (52.5% of theoretical) was filtered off. It was purified by repeated recrystallization from alcohol (1:35) or from glacial acetic acid (1:10) with the addition of a small volume of water. The dye melted with decomposition at 175-177°; with alcoholic alkali it gave a sky-blue coloration.

0.1102 g substance: 0.2342 g CO_2; 0.0398 g H_2O. 0.1054 g substance: 0.2261 g CO_2; 0.0390 g H_2O. 0.0995 g substance: 15.1 ml N_2 (20°, 750 mm). 0.0875 g substance: 13.2 ml N_2 (21°, 757 mm). Found %: C 58.45, 58.52; H 4.03, 4.15; N 17.3, 17.27. $C_{20}H_{17}O_5N_5$. Calculated %: C 58.69; H 4.1, N 17.12.

The same compound is obtained upon reaction of 1 mole p-nitrodiazobenzene with the azo dye obtained in the preceding instance.

Interaction of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine with p-sulfamidodiazobenzene. To the cooled solution of 2.6 g of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine and 5 g of anhydrous sodium acetate in 50 ml of glacial acetic acid was added a solution of p-sulfamidodiazobenzene, prepared from 1.72 g of sulfanilamide (dissolved in a mixture of 5.5 ml of concentrated hydrochloric acid and 7 ml of water) and 0.7 g of sodium nitrite (in the form of 25% solution). The mixture was stirred for 2-3 hours and left at room temperature for 14-16 hrs. The dark red solution was filtered, diluted with 4 times the volume of water, and the precipitate separated, washed with water, and dried at 50-60°. Yield 3.7 g (75.8% of theory). To purify, the precipitate was boiled with water, after drying extracted by cold acetone and the acetone driven off, crystallized from alcohol (1:25) or from 50% acetic acid (1:20). M.p. above 240°. Gave raspberry-red color with alcoholic alkali.

0.0952 g substance: 0.1882 g CO_2; 0.0391 g H_2O. 0.0804 g substance: 0.1592 g CO_2; 0.0342 g H_2O. 0.1210 g substance: 16.5 ml N_2 (20°, 757 mm). 0.0905 g substance: 12.7 ml N_2 (20°, 750 mm). Found %: C 53.92, 54.02; H 4.59, 4.76; N 15.63, 15.91. $C_{20}H_{21}O_5N_5S$. Calculated %: C 54.17; H 4.74; N 15.8.

Interaction of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine with p-nitrodiazobenzene. Azo-conjugation of 1.84 g of the initial substance was conducted at 0° in the manner described above for the phenyl analog. Yield 2.8 g (87.4% of theoretical). After purification with boiling water and extraction by ethyl acetate the product was recrystallized 3 times from alcohol (1:25) or from 70% acetic acid (1:15). From the alcoholic alkali the substance gave a blue color; m.p. 174-176°.

0.1020 g substance: 0.1883 g CO_2; 0.0428 g H_2O. 0.1104 g substance: 0.2033 g CO_2; 0.0441 g H_2O. 0.0910 g substance: 16.6 ml N_2 (21°, 763 mm). 0.1203 g substance: 21.7 ml N_2 (20°, 763 mm). Found %: C 50.34, 50.23; H 4.69, 4.47; N 21.06, 20.88. $C_{14}H_{15}O_5N_5$. Calculated %: C 50.45; H 4.5; N 21.02.

When this azo conjugation was conducted in 70 ml of glacial acetic acid and diazo solution, there was then formed 2.7 g (81% of theoretical) of brown azo dye. It was purified by extraction with cold acetone and crystallization from alcohol (1:15). It melted with decomposition at 185-187°; in alcoholic alkali it gave a dark-violet color.

0.1034 g substance: 0.1920 g CO_2; 0.0358 g H_2O 0.1074 g substance: 0.1991 g CO_2; 0.0386 g H_2O. 0.1416 g substance: 26.1 ml N_2 (22°, 760 mm). 0.1306 g substance: 24.8 ml N_2 (24°, 757 mm). Found %: C 50.65, 50.47; H 3.87, 4.02; N 21.03, 21.32. $C_{14}H_{13}O_5N_5$. Calculated %: C 50.75; H 3.92; N 21.14.

Interaction of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine with p-sulfamidodiazobenzene. 1.84 g of the initial substance and 5 g of anhydrous sodium acetate were dissolved in 60 ml of glacial acetic acid. At 0° the diazo solution prepared from 1.72 g of sulfanilamide was poured in. The reaction mixture was left to stand on ice for 14-16 hours. The dye was isolated by dilution of the filtered solution with water. Yield 2.9 g (79.6% of theoretical). The dye was purified as described above for the phenyl analog. The dye melted indefinitely above 260°; with alcoholic alkali it gave color.

0.0891 g substance: 0.1488 g CO_2; 0.0385 g H_2O. 0.1031 g substance: 0.1726 g CO_2; 0.0425 g H_2O. 0.0932 g substance: 15.5 ml N_2 (21°, 763 mm). 0.0972 g substance: 16.4 ml N_2 (20°, 757 mm). Found %: C 45.5, 45.66; H 4.78, 4.38; N 19.20, 19.31. $C_{20}H_{21}O_5N_5S$. Calculated %: C 45.77; H 4.63; N 19.13.

Bromination of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine [4,11]. To the exact weight of 2.6 g of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine suspended in 20 ml of chloroform was added a solution of 1.37 ml of bromine in 40 ml of chloroform. The mixture was stirred for 40 minutes at room temperature, and then for 30 minutes at boiling. The chloroform was driven off to a volume of 10 ml, and 25 ml of alcohol added, and the remaining chloroform distilled off with it. After cooling, the precipitate was filtered off and dried. Yield 3.5 g (83% of theoretical), m.p. 182-183° (with decomposition). The dibromide was purified by recrystallization from alcohol.

Bromination of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine. The initial substance (5.4 g) was suspended in 60 ml of chloroform, and 4.2 ml of bromine in 150 ml of chloroform added. The mixture was stirred for 20 minutes at room temperature, and then for 1 hour while boiling. The chloroform was driven off in vacuo to a volume of 10-15 ml, 30 ml of alcohol added, and distilled off again in vacuo to a volume of 10 ml. The remainder was left for 24 hrs in vacuo; the precipitate was then filtered off, washed with aqueous alcohol and dried in vacuo. Yield 7.28 g (70.6% of theoretical). The dibromide was recrystallized from 30% alcohol (1:5). It appeared as white, large crystals, soluble in alcohol, acetone, chloroform and acetic acid; m.p. 115-116° (with decomposition).

0.0892 g substance: 0.0915 g CO_2; 0.0284 g H_2O. 0.0918 g substance: 0.0948 g CO_2; 0.0291 g H_2O. 0.0964 g substance: 7.1 ml N_2 (20°, 748 mm). 0.1174 g substance: 8.4 ml N_2 (21°, 768 mm). Found %: C 27.99, 28.01; H 3.57, 3.61; N 8.38, 8.3. $C_8H_{12}O_2N_2Br_2$. Calculated %: C 27.9; H 3.48; N 8.14.

For debromination, the obtained dibromides were dissolved in alcohol (30 parts), 4 parts of zinc dust added, and boiled for 7 hours while stirring. The hot solution was filtered and the filtrate diluted with water. After a time the crystals of initial dihydropyrimidine precipitated.

Determination of the percentage of brominated isomers in the investigated dihydropyrimidines. The determination was carried out on the substances three times recrystallized from alcohol. The weighed portion of substance was dissolved in alcohol and an excess of freshly prepared, titrated, alcoholic bromine solution (approximately 10-12%) added. After a given bromination time an excess of potassium iodide was added as a 50% aqueous solution. The separated iodine was titrated by 0.1 N hyposulfite solution in the presence of starch. The determination was conducted twice in each case.

The percentage contents of brominated isomers (C) was calculated according to the following formula:

$$C = \frac{(a-b)\cdot M\cdot 100}{c\cdot 20000}$$

where a = number of ml of 0.1 N hyposulfite solution used for titration of the alcoholic bromine solution used; b = the number of ml of 0.1 N hyposulfite solution used for titration of the excess bromine remaining after bromination of the weighed portion of substance; c = weighed sample of analyzed substance; M = molecular weight of the analyzed substance.

Results of the determination are summarized in Tables 1 and 2.

Separation of the nonbrominable isomers. Rate of equilibrium attainment. The reaction mixture left after bromometric titration was diluted with double the volume of water. The nonbrominable isomer precipitated. The precipitate was washed with water and cold alcohol, and dried at room temperature. The dihydropyrimidines thus obtained did not completely absorb bromine upon treatment with the titrated solution of alcoholic bromine. Upon their boiling in a solution of alcohol or benzene the percentage contents of brominable isomers increased, and after 1 hour of boiling reached the equilibrium values given in Tables 1 and 2.

Derivation of N-acetyl-2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine. Its titration. 5.2 g of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine and 50 ml of acetic anhydride were boiled for 3 hours with a reflux condenser. The cooled solution was gradually diluted with 5 times its volume of water. The precipitated substance weighed 4.1 g (68.3% of theoretical). It was difficultly soluble in water, readily soluble in acetic acid, acetone, and hot alcohol (1:6), from which it crystallized in the form of light, white flakes; m.p. 176-177°.

0.1014 g substance: 0.2359 g CO_2; 0.0541 g H_2O. 0.0824 g substance: 0.1928 g CO_2; 0.0440 g H_2O. 0.1525 g substance: 12.4 ml N_2 (23°, 759 mm). 0.1220 g substance: 10.1 ml N_2 (22.5°, 768 mm). Found %: C 63.47, 63.84; H 6.0, 5.98; N 9.29, 9.46. $C_{16}H_{18}O_4N_2$. Calculated %: C 63.6. H 5.96; N 9.27.

TABLE 1

2-Hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine

Test No.	Temp. (in °C)	Duration of bromination (in minutes)	c (g)	a (ml)	b (ml)	M	C (in %)
1	0	5	0.2	23.5	20.5	260	19.5
2	0	5	0.2	24.4	20.5	260	18.85
3	0	15	0.2	23.6	20.6	260	19.5
4	0	15	0.2	23.5	20.4	260	20.15
5	17	5	0.2	27.45	24.3	260	20.47
6	17	5	0.2	27.5	24.4	260	20.15
7	17	15	0.2	27.6	24.5	260	20.15
8	17	15	0.2	27.8	24.6	260	20.8

TABLE 2

2-Hydroxy-4-methyl-5-carbethoxydihydropyrimidine

Test No.	Temp. (in °C)	Duration of bromination (in minutes)	c (g)	a (ml)	b (ml)	M	C (in %)
1	0	5	0.25	25.8	24.1	184	6.25
2	0	5	0.25	25.7	23.9	184	6.62
3	0	15	0.25	25.6	23.9	184	6.25
4	0	15	0.25	25.7	24.1	184	5.7
5	17	5	0.25	25.5	23.7	184	6.62
6	17	5	0.25	25.6	23.9	184	6.25
7	17	15	0.25	25.6	23.8	184	6.62
8	17	15	0.25	25.4	23.5	184	6.99

TABLE 3

N-Acetyl-2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine

Test No.	Temp. (in °C)	Duration of bromination (in minutes)	c (g)	a (ml)	b (ml)	M	C (in %)
1	0	5	0.25	28.6	12.4	302	97.9
2	0	5	0.25	28.8	12.5	302	98.5
3	0	15	0.25	28.6	12.2	302	99.1
4	0	15	0.25	28.5	12.3	302	97.9
5	17	5	0.25	28.7	12.4	302	98.5
6	17	5	0.25	28.5	12.1	302	99.1
7	17	15	0.25	28.4	11.9	302	99.7
8	17	15	0.25	28.2	11.7	302	99.7

Results of the bromometric determination of the obtained substance are summarized in Table 3.

Derivation of N-acetyl-2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine. Its titration. 3.68 g of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine and 36 ml of acetic anhydride were boiled for 3 hours with a reflux. After cooling the solution and diluting it with 7 times its volume of water, there was precipitated 2.8 g (61.9% of theoretical) of the solid. Crystallized from alcohol (1:20), water (1:100) or 50% acetic acid (1:10) in the form of long white needles (by slow cooling); m.p. 149.5-150.5°.

0.1187 g substance: 0.2304 g CO_2; 0.0651 g H_2O. 0.0802 g substance: 0.1562 g CO_2; 0.0442 g H_2O. 0.1274 g substance: 13.5 ml N_2 (24°, 760 mm). 0.1062 g substance: 11.4 ml N_2 (22°, 758 mm). Found %: C 52.9, 53.14; H 6.14, 6.17; N 12.03, 12.24. $C_{10}H_{14}O_4N_2$. Calculated %: C 53.09; H 6.19; N 11.9.

The dibromide of the given compound reacts in the cold with potassium iodide, separating iodine. Thus, upon titration, the excess of bromine was bound with β-naphthol [14,15], after which there was added a solution of potassium iodide, and after 4 hours the separated iodine was titrated with 0.1 N hyposulfite solution.

During titration of the 0.2 g weighed sample, after 5 minutes of bromination 17.6 ml of hyposulfite was consumed, from which $C = \frac{17.6 \cdot 226 \cdot 100}{0.2 \cdot 20000} = 99.44\%$ (226 - molecular weight). After 15 minutes of bromination there was consumed 17.7 ml of the hyposulfite solution, from which $C = \frac{17.7 \cdot 226 \cdot 100}{0.2 \cdot 20000} = 100.01\%$.

The obtained N-acetyl derivatives, and also the dibromoderivatives of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine and of 2-hydroxy-4-methyl-5-carbethoxydihydropyrimidine, were subjected to reaction with p-nitrodiazobenzene under the above-described conditions. In no case was azo conjugation observed; the initial substances were recovered unchanged.

Nitration of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine. 3.68 g of the initial substance was dissolved in 22 ml of concentrated sulfuric acid, 22 ml of 10% potassium nitrate solution in concentrated sulfuric acid was added, and the mixture obtained was allowed to stand for 4 hours at 40-45°. After cooling, the solution was poured into an equal volume of water, and the precipitated white product was filtered off, washed with water and dried at 50-55°. Yield 3.6 g (90% of theoretical). The nitrocarboxylic acid obtained was recrystallized from water (1:100), alcohol (1:10) or from 50% acetic acid (1:6). Long silky needles, soluble in alkali, carbonates and pyridine, with a yellow coloration. M.p. 142.5-143.5°. The salts of lead, copper, nickel and cobalt were hard to dissolve.

0.0940 g substance: 0.1235 g CO_2; 0.0371 g H_2O. 0.1039 g substance: 0.1361 g CO_2; 0.0340 g H_2O. 0.0810 g substance: 14.5 ml N_2 (20°, 763 mm). 0.0932 g substance: 17.2 ml N_2 (22°, 748 mm). Found %: C 35.83, 35.70; H 3.67, 3.66; N 20.74, 20.79. $C_6H_7O_5N_3$. Calculated %: C 35.82; H 3.48; N 20.89.

The substance was also able to conjugate in pyridine solution with p-nitrobenzene. Upon pouring the raspberry-red pyridine solution into diluted hydrochloric acid, the precipitate of brown azo dye separated.

Nitration of 2-hydroxy-4-methyl-5-carbethoxy-6-phenyldihydropyrimidine. To 5.2 g of the initial substance in 30 ml of concentrated sulfuric acid was added dropwise, with stirring, 30 ml of a 10% solution of potassium nitrate in concentrated sulfuric acid. After 1 hour the reaction liquid was poured into 15 times its volume of water. The precipitated white product was filtered off, washed with water, and dried in vacuo. Yield 6.41 g (99.5% of theoretical). After three recrystallizations from 50% acetic acid (1:20) its m.p. was 133.5-134.5°. The substance dissolved in alcohol, ether, and acetone. Soluble in alkali and carbonates with yellow coloration.

0.0812 g substance: 0.1334 g CO_2; 0.0241 g H_2O. 0.1025 g substance: 0.1675 g CO_2; 0.0301 g H_2O. 0.1034 g substance: 15.8 ml N_2 (21°, 766 mm). 0.1082 g substance: 16.8 ml N_2 (21°, 752 mm). Found %: C 44.81, 44.55; H 3.32, 3.28; N 17.57, 17.65. $C_{12}H_{10}O_7N_4$. Calculated %: C 44.72; H 3.13; N 17.39.

For transformation into the yellow isomer the obtained substance was dissolved in 0.1 N alkali, and a 1 N solution of hydrochloric acid was added dropwise at 0°. The yellow substance obtained, without melting, decomposed with a flash at 117-118°; soluble in alcohol, acetone, acetic acid, pyridine, aqueous alkali, and carbonates.

0.0812 g substance: 0.1325 g CO_2; 0.0222 g H_2O. 0.0817 g substance: 0.1336 g CO_2; 0.0232 g H_2O. 0.0988 g substance: 15.2 ml N_2 (22°, 755 mm). 0.1117 g substance: 17.4 ml N_2 (21°, 753 mm). Found %: C 44.5, 44.59; H 3.06, 3.17; N 17.49, 17.68. $C_{12}H_{10}O_7N_4$. Calculated %: C 44.72; H 3.13; N 17.39.

Oxidation of 2-hydroxy-4-methyl-5-nitro-5-carboxy-6-nitrophenyldihydropyrimidine. 3.22 g (0.01 mole) of 2-hydroxy-4-methyl-5-nitro-5-carboxy-6-nitrophenyldihydropyrimidine was dissolved in 100 ml of 5% potassium hydroxide solution. To the solution was gradually added, with heating, 12 g of potassium permanganate, and the mixture was then boiled for one hour and a half with a reflux. The colored solution was decolorized by a small volume of alcohol. The precipitate of manganese dioxide was filtered off and the colorless solution steamed off on a water bath to a volume of 50-60 ml, and acidified to Congo red with 5% hydrochloric acid. Immediately a slightly yellow precipitate separated. After washing with water and drying, the precipitate melted at 235-236°, and after a single crystallization at 238°. A mixture of the precipitate with an authentic sample of p-nitrobenzoic acid also melted at 238°. Thus it can be deduced that the initial compound has the structure (VI) (R = p-$O_2NC_6H_4$–).

Interaction of 2-hydroxy-4-methyl-5-nitro-6-nitrophenyldihydropyrimidine-5-carboxylic acid with p-nitrodiazobenzene. 6.44 g of the dinitro acid (both white and yellow) was dissolved in 40 ml of pyridine and to the solution was added 1 mole of p-nitrodiazobenzene. The solution immediately turned dark-red. After 2 hrs it was poured in 700 ml of 5% hydrochloric acid. The bright red azo dye obtained from the white dinitro acid, was crystallized 3 times from 1.5% alcoholic hydrochloric acid (1:12). M.p. 173-175°. Soluble in alcohol, acetone, pyridine, and acetic acid. In alcoholic alkali its color becomes dark-red.

0.0835 g substance: 0.1406 g CO_2; 0.0191 g H_2O. 0.1086 g substance; 0.1816 g CO_2; 0.0273 g H_2O. 0.1012 g substance: 18.5 ml N_2 (22°, 755 mm). 0.0930 g substance: 17.1 ml N_2 (23°, 753 mm). Found %: C 45.83, 45.61; H 2.52, 2.81; N 20.81, 20.75. $C_{18}H_{12}O_9N_7$. Calculated %: C 45.86; H 2.76; N 20.8.

The brown dye, obtained from the yellow dinitroacid, was purified by crystallization from 1.5% alcoholic hydrochloric acid (1:125). M.p. 204-206°. In alcoholic alkali, it gave the same coloration as the preceding dye.

0.1106 g substance: 0.1868 g CO_2; 0.0260 g H_2O. 0.1023 g substance: 0.1712 g CO_2; 0.0242 g H_2O. 0.0801 g substance: 14.5 ml N_2 (21°, 763 mm). 0.0906 g substance: 16.5 ml N_2 (21°, 763 mm). Found %: C 46.12, 45.66; H 2.63, 2.65; N 20.91, 21.03. $C_{18}H_{13}O_9N_7$. Calculated %: C 45.86; H 2.76; N 20.8.

The dye obtained from the white dinitroacid, after dissolution in alkali and subsequent acidification, transformed into the dye obtained from the yellow dinitroacid.

Reaction of bromine with 2-hydroxy-4-p-nitrobenzeneazomethyl-5-carbethoxy-6-phenyldihydropyrimidine. 2.1 g of the dye was dissolved in 60 ml of dry chloroform and 2.4 g of bromine, dissolved in chloroform was added. After prolonged boiling, the chloroform was distilled off and 60 ml of alcohol was added. Upon cooling, from the solution separated the initial dye, not containing bromine; its mixture with the initial dye gave no depression of melting point.

SUMMARY

1. The activity of the methyl group in six-membered heterocycles, containing two double bonds in the ring, was studied, namely, in the monohydroxydihydropyrimidines. It was shown that the methyl group in the investigated compounds possesses high activity, sufficient for condensation with aldehydes and diazo compounds.

2. It was demonstrated that the dihydropyrimidines, obtained by the Biginelli condensation, are represented as an equilibrium mixture of tautomers, the relative quantity of which is determined by the bromometric method.

3. The structural formula proposed by Biginelli for the dihydropyrimidines does not conform to the displayed activity of the methyl group.

4. Tautomers incapable of bromination were isolated in the free state. Upon boiling in alcohol, benzene, or glacial acetic acid, they are again transformed into an equilibrium mixture of tautomers with constant composition.

5. The derivation of N-acetyl derivatives, their ability to combine with bromine, and their inability to conjugate with diazo compounds confirm that the active methyl group exists in only one definite tautomeric form of the dihydropyrimidines. The proposed structural formula for this tautomer explains the observed activity of the methyl group in the investigated dihydropyrimidines.

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THE SYNTHESIS OF 3,4-BENZOPYRENE AND 3,4,6,7-DIBENZOPYRENE FROM PHENALONE-9 AND BENZANTHRONE*

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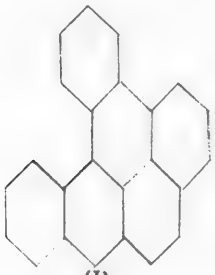
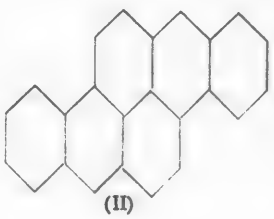
One of the most actively investigated carcinogenic substances is 3,4-benzopyrene, to which more than 200 works had been devoted by 1941. As regards the hexa-nuclear hydrocarbons and the hydrocarbons with a large number of condensed nuclei, much less material exists.

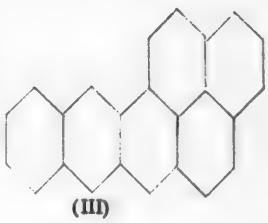
In the period 1935-1941 there were synthesized and investigated for carcinogenic activity some dibenzopyrenes and naphthobenzopyrenes. 1,2,3,4-Dibenzopyrene (I) [1] and 3,4,8,9-dibenzopyrene (II) [2]** showed considerable carcinogenicity, while at the same time 2', 3' -naphtho-3,4-pyrene (III) proved to be inactive [3].



(I)

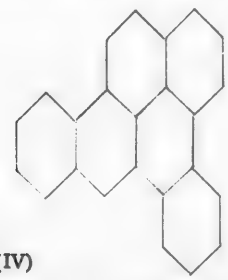


(II)

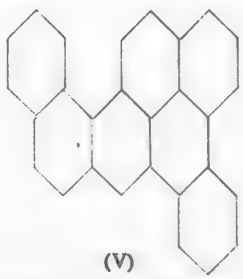


(III)

In 1941, A. E. Arbuzov and N. P. Grechkin [4] synthesized 3,4,6,7-dibenzopyrene (IV) and 1', 2', 3', 4'-naphtho-6,7-benzopyrene (V) for the purpose of explaining the influence of structure upon carcinogenicity of hexa-nuclear hydrocarbons, and the possibility for carcinogenicity of hepta-nuclear compounds.



(IV)



(V)

The war temporarily interrupted the investigations, both in the synthesis of the polynuclear hydrocarbons and in the testing of their carcinogenicity, in favor of training physicians, conducted by N. I. Vylegzhanin at the Kazan State Institute. After termination of the war, these researches were resumed and interesting data were soon obtained. At the present time it is possible to consider as fully proven the high blastomogenic activity of both hydrocarbons. Tests conducted by N. I. Vylegzhanin on white mice have demonstrated the very high blastomogenic activity of 3,4,6,7-dibenzopyrene, forming both sarcomas and cancerous tumors. On the basis

* Results reported during the session of the Division of Chemical Sciences, Academy of Sciences, USSR and Academy of Sciences of the Ukraine, USSR, in Kiev, June 1950; see the Annals of the Academy of Sciences, Division of Chemical Sciences 552 (1950).

** Evidently the same hydrocarbon, under the name of 1,2,6,7-dibenzopyrene, was investigated by Voronyansky, Pisareva and Sorin [10], because Zilberman [9], having synthesized this hydrocarbon, gave it the formula (II), although the m.p. of Zilberman's sample was higher by 17° than that of hydrocarbon (II).

of N. I. Vylegzhanin's data, 3,4,6,7-dibenzopyrene can be placed in the same group with such strong blastomogenic substances as 3,4-benzopyrene and 20-methylcholanthrene. It should be noted that 3,4,6,7-dibenzopyrene was found to be non-toxic for white mice, which facilitates work with it.

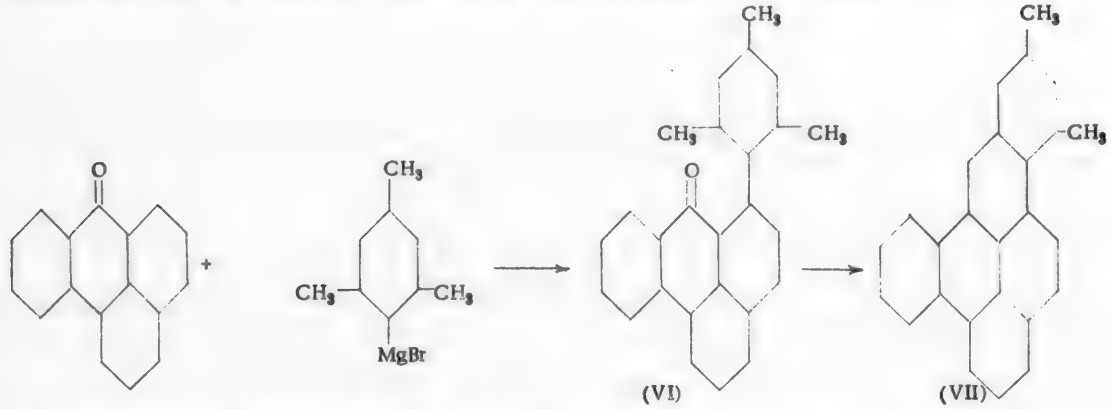
Within two years after publication of the article on the synthesis of 3,4,6,7-dibenzopyrene, Clar [5] described its synthesis by an entirely different, more complicated method, starting with 1,2,3,4,5,6,7,8-octahydroanthracene, through the 10-benzoyl derivative. The Clar synthesis is complex and accompanied by isomerizations, and along with 3,4,6,7-dibenzopyrene there is obtained 1,2,6,7-dibenzopyrene, which is separated by recrystallization of the picrates. The melting point of Clar's 3,4,6,7-dibenzopyrene is 14° lower, which can be explained either by insufficient purity of the Clar sample, or by a different method of melting point determination. Clar makes no reference to carcinogenicity test data.

No less interesting data were obtained by N. I. Vylegzhanin with 1', 2', 3,4-naphtho-6,7-benzo-pyrene,, containing 7 nuclei. The hydrocarbon was found to be blastomogenic, inducing the appearance of sarcomas and leukemia.

The data cited on the blastomogenic action of 3,4,6,7-dibenzopyrene and 1', 2', 3,4-naphtho-6,7-benzo-pyrene stimulated the authors to continue the work on synthesis of various polynuclear hydrocarbons of the 3,4, 6,7-dibenzopyrene type. Certain of the obtained results are reported in the present article.

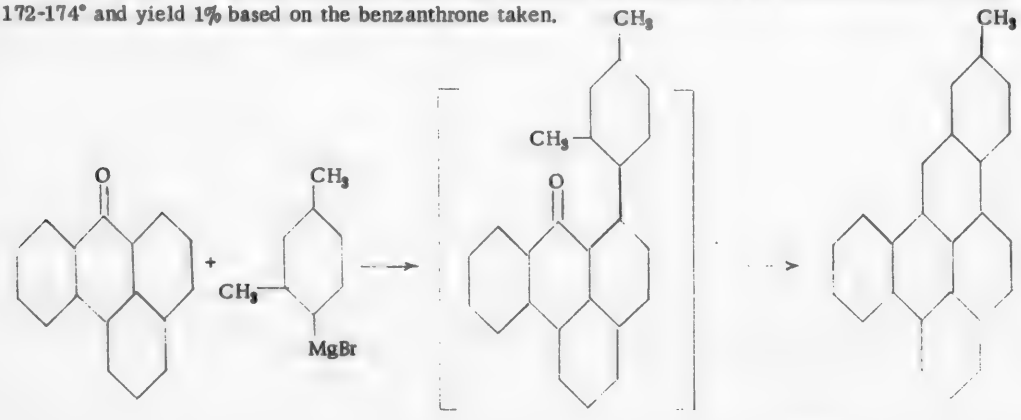
For the synthesis of derivatives of 3,4,6,7-dibenzopyrene, the authors used the earlier applied method of reaction of arylmagnesium halide with benzanthrone, containing a methyl or methylene group in the ortho position, leading to 4-substituted benzanthrones, with subsequent pyrolysis of the ketone obtained, according to Elbs.

Upon reaction of mangesiumbromomesitylene with benzanthrone there was obtained, with a yield 59% of theoretical, ketone (VI), with a m.p. of 167-168.5°, which, upon pyrolysis, gave the dimethyl derivative of 3,4,6,7-dibenzopyrene (VII), m.p. 166-167.5°, with a yield of 11% based on mesitylbenzanthrone.



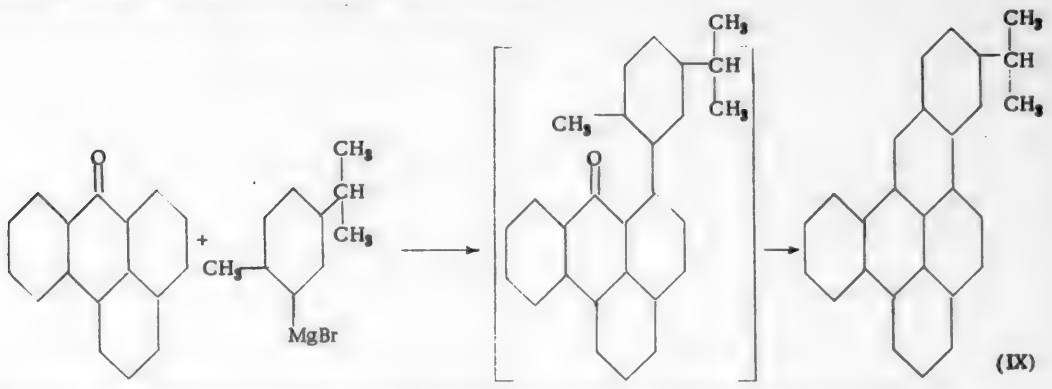
(VI) (VII)

Reaction of 1,3-dimethyl-4-magnesiumbromobenzene with benzanthrone, followed by pyrolysis of the ketone, which could not be isolated in the free state, led to the isolation of 3-methyl-3,4,6,7-dibenzopyrene (VIII), m.p. 172-174° and yield 1% based on the benzanthrone taken.



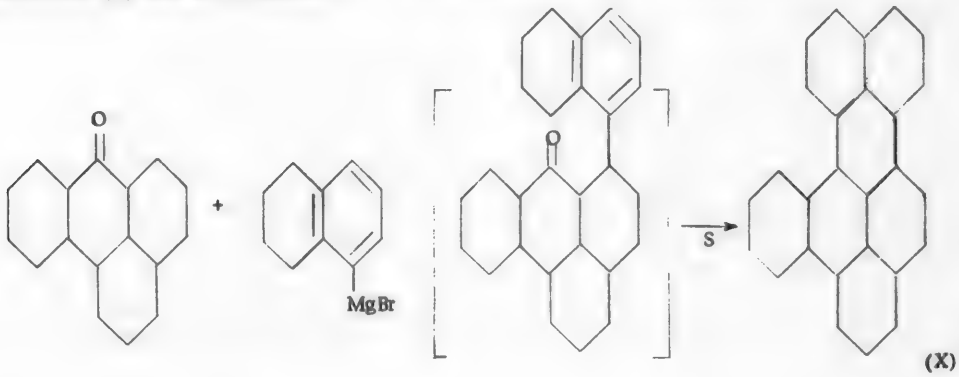
(VIII)

By a similar procedure, upon reaction of 2-mangesiumbromocymene with benzanthrone there was obtained the isopropyl derivative of 3,4,6,7-dibenzopyrene (IX), m.p. 124.5-126.5°. Cymylbenzanthrone could not be separated in the pure state, and the crude reaction product was pyrolized.



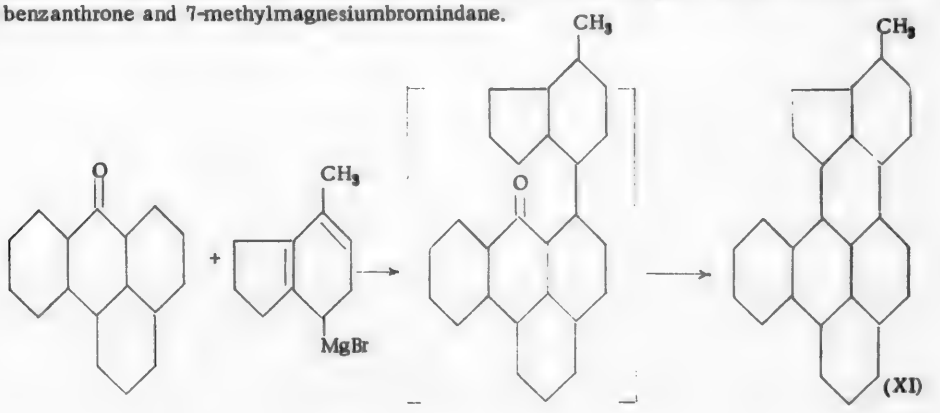
(IX)

Upon reaction of α-magnesiumbromotetraline with benzanthrone there was obtained a hard noncrystalline product. Its pyrolysis, with subsequent dehydration by sulfur, led to isolation of an insignificant yield (3%) of 3,4,5,6,7-tribenzopyrene (X) with m.p. 206-207°.



(X)

An interesting hydrocarbon was synthesized by the authors upon reaction of 7-methyl-4-magnesiumbromindane with benzanthrone followed by pyrolysis of the ketone, which could not be isolated in the pure state. As a result of the pyrolysis there was obtained hydrocarbon (XI), m.p. 241-242.5°, with a 12% yield for the raw reaction product between benzanthrone and 7-methylmagnesiumbromindane.



(XI)

Hydrocarbon (XI) (3'-methyl-4',5-ethylene-3,4,6,7-dibenzopyrene) is of particular interest since it contains within itself the framework of some of the strongest carcinogens: 3,4-benzopyrene, 20-methylcholanthrene and 9,10-disubstituted 1,2-benzanthracene. Experiments testing its blastomogenic action, conducted by N. I. Vylegzhanin,

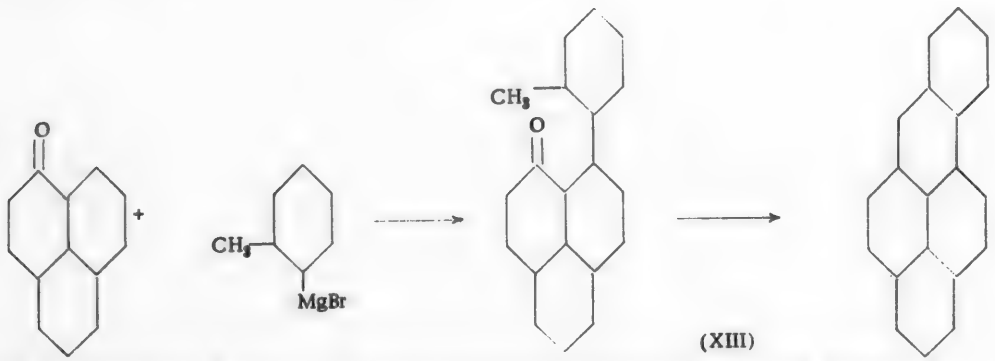
have shown that it possesses weak blastomogenic, but intense frank leukemic, action.

Syntheses of the polynuclear hydrocarbons are found, as a rule, to be multistage. The method applied by the authors, using benzanthrone, though it gives small yields of final products, is based upon the utilization of accessible, technical benzanthrone, and includes only 2 steps.

It was of interest to clarify the feasibility of a similar kind of synthesis of derivatives of 3,4-benzopyrene through phenalone-9 (XII).

Koelsch and Anthes [6] demonstrated that the reaction of organo-magnesium compounds with phenalone-9 leads to 1-substituted phenalones-9, through the intermediate formation of a dihydro derivative.

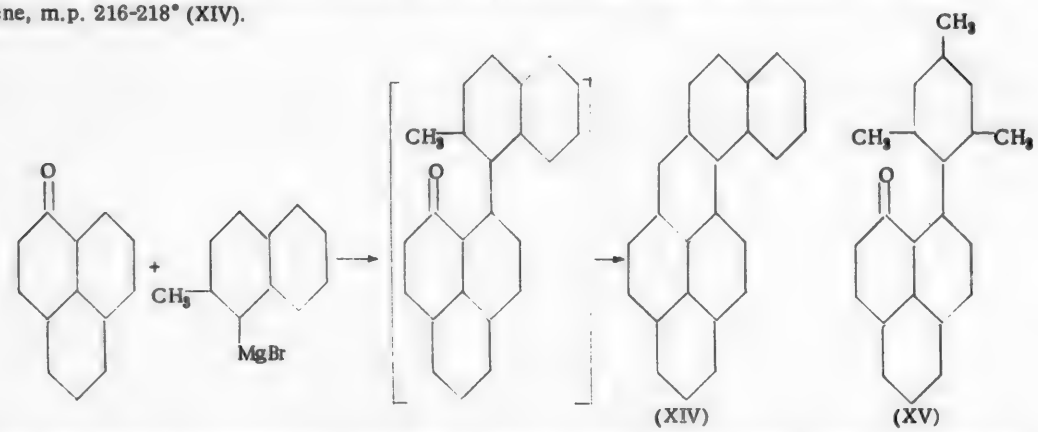
Reaction of o-magnesiumbromotoluene with phenalone-9, with subsequent pyrolysis of the ketone formed, should lead to 3,4-benzopyrene.



(XIII)

Tests conducted by the authors have shown that, upon reaction of o-magnesiumbromotoluene with phenalone-9, there is obtained, with a yield 49% of the theoretical, the ketone (XIII) (1-o-tolyl-9-phenalone), with a m.p. of 156-157°, which, upon pyrolysis, gives 3,4-benzopyrene. However, the pyrolysis gives an insignificant yield of pure 3,4-benzopyrene.

In analogous fashion, upon reaction of α-magnesiumbrom-β-methylnaphthalene with phenalone-9, with subsequent pyrolysis of the ketone, isolation of which was not accomplished, there was obtained 1', 2', 3,4-naphthopyrene, m.p. 216-218° (XIV).



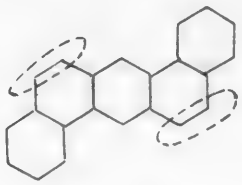
(XIV) (XV)

Reaction of magnesiumbromomesitylene with phenalone-9 leads to the formation of ketone (1-mesitylphenalone-9) (XV) in 66% of the theoretical yield, m.p. 169-171°. Its pyrolysis, however, gave a negligible amount of a compound with m.p. 213-215°, which we have not yet carefully analyzed

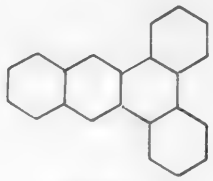
High carcinogenicity of the 3,4,6,7-dibenzopyrene synthesized by A. E. Arbuzov and N. P. Grechkin is found to be in contradiction with the declared opinion of Pullman [7] concerning the connection between carcinogenic activity and an increased electronic density in a certain orbital region of the molecule of a carcinogenic substance, corresponding to the 9,10-position of the phenanthrene skeleton in the "K" orbit.

The activity of 1,2,5,6-dibenzanthracene, according to Pullman, is connected with the presence of the "K"

orbit in the molecule (XVI). Substitution in the "K" orbital region of 1,2,3,4-dibenzanthracene (XVII) leads to loss of the carcinogenic activity.



(XVI)



(XVII)

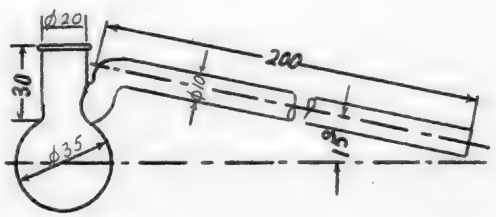
3,4,6,7-Dibenzopyrene and its derivatives could be regarded as derivatives of 1,2-benzanthracene, in which the "K" orbit is substituted. At the same time the hydrocarbon obtained was found to be highly carcinogenic. It is true that there is another "K" orbit region that has preserved the 9,10-position of the phenanthrene nucleus, but it obviously comes closer to the chrysenic grouping, inactive in the sense of carcinogenicity.

On the other hand, 2', 3'-naphtho-3,4-pyrene, where the "K" and "K_1" orbital regions are free, were found to be non-carcinogenic, as was indicated at the beginning of the present article.

EXPERIMENTAL

Reaction of 7-methyl-4-magnesiumbromindane with 1,9-benzanthrone-10. To 1.7 g of magnesium in 50 ml of ether was added a few drops of ethyl bromide; after reaction was started, there was added to the flask 15 g of 4-bromo-7-methylindane [8]. The reaction mass was boiled for 18 hours during that time the greater portion of the magnesium dissolved. Into the cooled mixture, at room temperature, was sprinkled 8 g (half the calculated quantity) of finely-ground benzanthrone (m.p. 169-170°). Upon adding the benzanthrone, local boiling of the ether resulted. After all of the benzanthrone had been added, the mixture was boiled for 3 hours; the ether was subsequently driven off and replaced by benzene; and the mixture was again heated to boiling for 5 hours. After cooling, followed by decomposition with water and dilute acetic acid, the benzolic layer was separated and subjected to steam distillation; residue – 8 g of orange-colored tar resembling sealing wax. During unsuccessful attempts, to crystallize the obtained product, there was isolated 1.5 g of unreacted benzanthrone. The remainder was dried in vacuo to the solid state and this form was subjected to pyrolysis.

Pyrolysis of the product obtained by reaction of 4-magnesiumbromo-7-methylindane with 1,9-benzanthrone-10. 6.2 g of the substance was divided into 4 equal portions, which were individually subjected to pyrolysis. Each 1.5 g of initial product was placed in a small flask of heat-resisting glass, with a low, wide outlet fused into the base of the neck; the dimensions of the flask are visible in the attached drawing.



Pyrolysis was conducted in a bath of Wood's alloy at 380-410° for 30-40 minutes. After evolution of water ceased, the pyrolysis products were distilled in vacuo at 2-3 mm, the bath temperature during distillation being 420-460°. 0.5 g of hard transparent distillate was obtained.

The remaining initial substance was reprocessed under the same conditions. In all there was obtained 1.8 g of hard distillate. After a series of recrystallizations from benzene there was obtained 0.68 g of pure crystalline substance in the form of thin yellow needles, m.p.241-242.5°. Yield was 7.0% of the theoretical,

on the basis of benzanthrone reacted.

0.0936 g substance: 0.3247 g CO_2; 0.0460 g H_2O. Found %: C 94.58; H 5.46. $C_{27}H_{18}$. Calculated %: C 94.78; H 5.27.

Reaction of magnesiumbromomesitylene with 1,9-benzanthrone-10. Into an ether solution of magnesiumbromomesitylene, prepared from 50 g of bromomesitylene and 6 g of magnesium in 150 ml of dry ether, there was sprinkled at room temperature 25 g (less than half the calculated quantity) of finely-pulverized benzanthrone. Time of addition was 40 minutes.

Reaction was accompanied by heat evolution. The ether boiled without external heating. When all of the benzanthrone had been added, the mixture was boiled for 1 hour. After decomposition of the cooled mixture with ice and dilute acetic acid, crystals precipitated immediately, which were filtered off. After separation of the ether layer and driving off of the ether, there was obtained an additional quantity of crystals. The total of crude substance was 33 g. After its recrystallization from benzene, there was obtained 22.3 g of yellow crystals, m.p. 167-168.5°. Yield 59% of theoretical, on the basis of benzanthrone.

0.1115 g substance: 0.3657 g CO_2; 0.0584 g H_2O. Found %: C 89.47; H 5.82. $C_{26}H_{20}O$. Calculated %: C 89.60; H 5.80.

Pyrolysis of 4-mesityl-1,9-benzanthrone-10. 14 g of mesitylbenzanthrone was subjected to pyrolysis in five approximately equal portions. Pyrolysis was conducted at a temperature of 380-410° for 30-40 minutes. The pyrolysis products were subjected to distillation under a vacuum of 2-3 mm, the bath temperature during distillation being 410-430°. The total obtained was 6 g of hard transparent distillate. After a series of recrystallizations from benzene, there was obtained 0.92 g of light yellow crystals, in the form of small needles. M.p. 166-167.5°. Yield 10.2%, based on mesitylbenzanthrone. Picrate from alcohol, m.p. 194-196°.

Analysis of the substance with m.p. 166-167.5°.

0.1204 g substance: 0.4173 g CO_2; 0.0601 g H_2O. Found %: C 94.52; H 5.55. $C_{26}H_{18}$. Calculated %: C 94.52; H 5.48.

Reaction of 2-mangesiumbromoparacymene with 1,9-benzanthrone-10. To the ether solution of 2-magnesiumbromoparacymene, obtained from 50 g o-bromoparacymene and 5.5 g of magnesium in 150 ml of dry ether, was added, portionwise over 30 minutes, 20 g of finely-powdered benzanthrone (40% of the calculated weight). The ether boiled at the expense of the heat evolved during the reaction. The reaction mass was boiled on a water bath for 1 hour, and after 1 hour was decomposed with water and dilute acetic acid. The ether layer was separated and distilled. After the previous distillations of ether with steam, there was obtained 31 g of orange-colored tar residue resembling sealing wax, soluble in many of the organic solvents, but non-crystallizable from any of them.

Pyrolysis of 4-(paracymene)-1,9-benzanthrone-10. 18 g of resinous product, obtained by the reaction of magnesiumbromoparacymene with benzanthrone, was subjected to pyrolysis in six 3-gram portions. The pyrolysis was carried out in a bath of Wood's metal at a temperature of 380-410° for 20-25 minutes (cessation of water evolution). The pyrolysis products were distilled from the flask of above-designed construction at a vacuum of 2-3 mm; temperature of distillation, 360-430°. As a result of the distillation there was obtained 5.6 g of a hard, transparent substance. After treatment of a solution of the distillate in benzene with the calculated weight of picric acid, there was obtained 5 g of picrate in the form of cherry-colored needles, m.p. 165-169° (recrystallized from alcohol-benzene). The hydrocarbon isolated by decomposition of the picrate after a few recrystallizations (from benzene-alcohol mixture) had a m.p. of 124.5-126.5°. Yield was 1 g or 5.5% of theoretical, on the basis of the benzanthrone entered into reaction.

0.1053 g substance: 0.3653 g CO_2; 0.0516 H_2O. Found %: C 94.62; H 5.45. $C_{27}H_{20}$. Calculated %: C 94.17; H 5.83.

Reaction of α-magnesiumbromotetralin with 1,9-benzanthrone-10. 12 g of finely ground benzanthrone was added to a solution of magnesiumbromotetralin, obtained from 22 g of the bromide and 2.5 g of magnesium in 100 ml of dry ether. Upon addition of the benzanthrone, the ether boiled up, and the benzanthrone changed into a solution, acquiring a brown pigmentation with green fluorescence. After all of the benzanthrone had been added, there appeared a dark oil on the bottom of the flask. The flask was further heated to boiling of the solvent for 2 hrs. After decomposition with water and dilute acetic acid there was obtained a dark oil which

was subjected to steam distillation. As a result of the distillation, there was obtained 14.2 g of hard, sealing wax-like tar, which could not be crystallized. This product was directly subjected to further pyrolysis.

Pyrolysis of the product obtained by the reaction of 2-magnesiumbromotetralin with benzanthrone. 10 g of the resinous product was pyrolyzed in three portions at a temperature of 360-390° for 20-25 minutes. The product of the pyrolysis was distilled on a Wood's metal bath under a 2-3 mm vacuum; the maximum temperature in the bath was 500°. There was obtained 6 g of hard distillate, which was dehydrated with sulfur (the theoretical amount of sulfur was taken, considering the distillate as pure substance). The mass obtained after dehydration was resubjected to distillation, as the result of which there was obtained 2 g of hard distillate. After multiple recrystallizations from benzene-alcohol mixture, there was obtained 0.15 g of substance in the form of light yellow needles, with m.p. 206-207°. From the mother liquor of the last recrystallization, there was obtained also 0.06 g of the substance, with a m.p. of 205.5-207°.

0.0193 g substance: 0.0676 g CO_2; 0.0077 g H_2O. Found %: C 95.50; H 4.43. $C_{27}H_{16}$. Calculated %: C 95.28; H 4.72.

Reaction of magnesiumbromo-m-xylol with benzanthrone. To an ether solution of magnesium bromo-m-xylol, taken in excess, was added 20 g of pulverized benzanthrone. Upon addition of the benzanthrone, the ether boiled up and the solution finally heated up to boiling. After 1 hour and a half of boiling, the cooled solution was decomposed with water and dilute acetic acid. The water layer was separated and the solution subjected to steam distillation. In the residue was a sealing wax-like mass, of brown color; weight after drying was 30 g. The substance was soluble in the usual organic solvents, but did not recrystallize from any of them.

Pyrolysis of the product obtained by reaction of magnesium-m-xylol with benzanthrone. 17.9 g of the resinous product was subjected to pyrolysis at a temperature of 390-420° for 20 minutes. The product of pyrolysis was extracted with benzene. To the benzene extract was added an alcoholic solution of picric acid, calculated on the hydrocarbon content of 50% of the product taken from pyrolysis. The isolated picrate (2.5 g) failed to purify. From the products of decomposition of the picrate with ammonia, after a series of recrystallizations from benzene-methanol mixture, the isolation of a yellow-gray crystalline substance, m.p. 172-174°, was successful. Yield 0.15 g, about 1% of the theoretical, on the basis of benzanthrone.

0.0139 g substance: 0.0485 g CO_2; 0.0062 g H_2O. Found %: C 95.15; H 4.96. $C_{25}H_{16}$. Calculated %: C 94.93; H 5.07.

Reaction of o-magnesiumbromotoluene with phenalone-9. To an excess (three times the calculated weight) of o-magnesiumbromotoluene in ether solution (21.90 g of bromotoluene, 3 g magnesium and 100 ml of ether) there was added 7.7 g of phenalone-9. Upon addition of the ketone, considerable heating up occurred and the ether boiled up, the solution acquiring a dark-red color. After boiling for half an hour, the cooled solution was decomposed with ice and acetic acid.

After driving off the solvent and toluene with steam, the residue crystallized; 11.6 g of raw substance was obtained. After recrystallization from benzene and from acetic acid, there was obtained 5.7 g (or 49% of the theoretical) of a substance with a m.p. of 156-157°.

0.0905 g substance: 0.2923 g CO_2; 0.0483 g H_2O. Found %: C 88.08; H 5.92. $C_{20}H_{16}O$. Calculated %: C 88.22; H 5.88.

Pyrolysis of 1-o-tolylphenalone-9. 4 g of ketone was subjected to pyrolysis at 360-380° for 30 minutes. The pyrolysis products were distilled in vacuo (2-3 mm); temperature of distillation 370-410°. 0.6 g of crystalline distillate was obtained. After a few recrystallizations, there was obtained 0.15 g of 3,4-benzopyrene with m.p. 174-176°. Yield 4% of theoretical.

Reaction of α-magnesiumbromo-β-methylnaphthalene with phenalone-9. To the ether solution of α-magnesium-bromo-β-methylnaphthalene, obtained from 20 g of α-bromo-β-methylnaphthalene and 2 g of magnesium (both substances taken in double the quantity as regards phenalone-9) was added by portions 8.5 g of finely-ground phenalone-9. Upon addition of the ketone, the ether boiled up and the ketone turned into a solution. Time of addition was 30 minutes. The solution was further heated to boiling for 1.5 hrs. After cooling, the reaction mixture was decomposed with ice and dilute acetic acid. As the result of driving off the ether, and steam distillation of the residue, there was obtained 16.8 g of hard sealing wax-like resin, brown in color. Attempts to isolate pure β-methylnaphthylphenalone-9 were unsuccessful.

Pyrolysis of the product obtained by reaction of α-magnesium-bromo-β-methylnaphthalene with phenalone-9. 12 g of the sealing wax-like product was subjected to pyrolysis in six portions, at a temperature of 370-400° for 20 minutes. The main bulk of water was eliminated at 370-390°. Upon completion of pyrolysis, the residue in the flask was distilled in vacuo (3 mm), temperature of the distillation 390-435°; at the outlet tube of the flask the distillate partially crystallized In all there was obtained 2.6 g of highly impure crystalline substance. After recrystallization from benzene-methanol mixture there was obtained 1.2 g of yellow crystals in the form of small flakes, with a m.p. 204-209°. After a few recrystallizations there was separated 0.8 g of crystals with a m.p. of 216-218°.

0.0931 g substance: 0.3252 g CO_2; 0.0419 g H_2O. Found %: C 95.30; H 5.02. $C_{24}H_{14}$. Calculated %: C 95.36; H 4.64.

Reaction of magnesiumbromomesitylene with phenalone-9. To an ether solution of magnesiumbromomesitylene (threefold excess), obtained from 38.8 g of bromomesitylene and 4.0 g of magnesium in 170 ml of ether, was added 10 g of phenalone-9, in powder form. There occurred quite a vigorous reaction, as a result of which the ether boiled up. After boiling for 1 hour, and decomposing the cooled mixture with water and dilute acetic acid, the total was subjected to steam distillation. As a result there was obtained a crystalline residue, contaminated by resinous substances. After a series of recrystallizations from glacial acetic acid, there was obtained 12 g of the substance with a m.p. of 160-171° (yield 66% of theoretical).

0.0780 g substance: 0.2529 g CO_2; 0.0451 g H_2O. Found %: C 88.41; H 6.43. $C_{22}H_{16}O$. Calculated %: C 88.59; H 6.04.

Pyrolysis of 1-mesitylphenalone-9. 10 g of 1-mesitylphenalone-9 was subjected to pyrolysis in five portions, at a temperature of 370-400° for 25 minutes. At the end of this time, the products of pyrolysis underwent distillation in vacuo (2-3 mm); temperature of the bath 390-420°. After multiple recrystallizations from benzene-methanol mixture, there was obtained 0.03 g of substance with m.p. 213-215°. Yield negligible.

SUMMARY

1. As the experiments of Vylegzhanin have demonstrated, 3,4,6,7-dibenzopyrene and 1',2', 3,4-naphtho-6,7-benzopyrene , previously synthesized by Arbuzov and Grechkin, have been shown to possess high blastomogenic activity, which spurred the synthesis of derivatives of 3,4,6,7-dibenzopyrene.

2. Corresponding 4-substituted-benzanthrones have been synthesized by reaction of benzanthrone with organomagnesium compounds containing the methyl or methylene group in the o-position. By pyrolysis of the latter, derivatives of 3,4,6,7-dibenzopyrene have been obtained.

Thus 3-methyl-3,4,6,7-dibenzopyrene, 1', 3'-dimethyl-3,4,6,7-dibenzopyrene, 2'-isopropyl-3,4,6,7-dibenzopyrene, 3'-methyl-4',5-ethylene-3,4,6,7-dibenzopyrene and 3,4,6,7-tribenzopyrene have been synthesized.

3. In similar fashion, starting with phenalone-9 through 1-substituted phenalones by pyrolysis, were synthesized 3,4-benzopyrene, and 1',2',3,4-naphthopyrene (not described in the literature).

4. The high carcinogenic activity of 3,4,6,7-dibenzopyrene and the inactivity of 2',3'-naphtho-3,4-pyrene contradict the opinions of Pullman concerning the connection between carcinogenicity and the presence of a specific "K" orbit region in the molecule of the carcinogenic substance, with an increased density of π-electrons.

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CYCLIZATION IN THE HALOUREIDE SERIES

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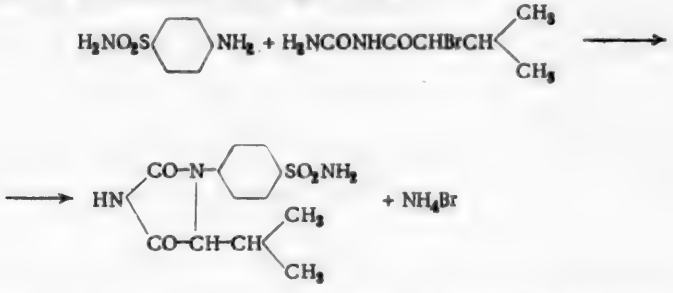
It has been pointed out that para-sulfamidophenylglycine (sulfaglycine) is considerably more effective against hemolytic streptococci than is sulfanilamide [1,2]. Its curative action on pneumonia has been demonstrated. The author has set as his goal the isolation of homologs of "sulfaglycine". By interaction of α-bromopropionic acid with sulfanilamide, in the presence of sodium hydroxide and sodium acetate, the corresponding compound is obtained with comparative ease; the yield, however, is small, because this substance is characterized by high solubility in water.

The method indicated above is not applicable to the isolation of the analogous compound from sulfanilamide and α-bromoisovaleric acid. All attempts to obtain this compound by the usual methods were unsuccessful. The author decided to fuse together sulfanilamide (m.p. 164°) with the ureide of α-bromoisovaleric acid (bromoural). The ureide of "sulfavaline" was of considerable interest in itself; from it can be obtained, without difficulty, "sulfavaline" itself.

The mixture of sulfanilamide with bromoural (m.p. 150°) melts at 130-135°. After about 45 minutes, the mass begins to thicken; within 2-2.5 hours it becomes completely hard, which demonstrates that the melting point of the product formed exceedsconsiderably the melting points of the ingredients. It should be noted that condensation is accompanied by considerable heat evolution.

If the process were to proceed in a normal fashion, the nitrogen content of the condensation product would be 17.83%. Analysis shows that the compound produced contains 14.32% nitrogen, which is 20% lower than that calculated on the assumption of a normal condensation. Because, on a percentage basis, the greatest nitrogen content is in the ureide part of the molecule, and thus the most vulnerable part, the hydrogen loss should be sought for here. Solution of the melt in sodium hydroxide was accompanied by considerable ammonia evolution. These circumstances prompted us to propose the following reaction:



This combination corresponds exactly with the percent nitrogen, carbon and hydrogen found.

The compound obtained could be regarded as hydantoin, where the N-hydrogen (in position 1) is substituted by sulfamidobenzene, and the C-hydrogen (in position 5) is substituted by the isopropyl radical.

From sulfanilamide and adaline (the ureide of bromodiethylacetic acid) an analogous product was obtained.

EXPERIMENTAL

8.5 g (1/20 mole) of sulfanilamide and 11 g (1/20 mole) of bromoural were melted together in a round-bottomed flask of 50-100 ml capacity, placed in an oil bath. At 130-135° the mixture melted. After approximately 45 minutes, the mixture began to thicken, and the temperature slowly rose to 150-155° in the mass (bath temperature 135-140°). Within 2.5 hours the reaction mass was completely hard, and reaction was complete. The melt was dissolved in a 3% solution of sodium hydroxide. When all of the melt was dissolved, activated carbon was added; the mixture was stirred for about a half-hour at 40-50°. The solution was then filtered and supersaturated with 10% hydrochloric acid. The precipitate was filtered off, washed with water to free it from

the hydrochloric acid and from the mineral salts, and dried. The dried product was extracted 2-3 times with hot chloroform. The precipitate filtered from the chloroform was boiled in a mixture of methanol (300 ml) and water (150 ml) in the presence of activated carbon. After 1/2 hour it was filtered off; from the filtrate upon cooling, there precipitated large white crystals. M.p. 256°. Yield of crude product ~9 g. Yield of pure sample was 7.5 g (the mother liquor was not utilized).

3.358 mg substance: 5.954 mg CO_2; 1.655 mg H_2O. 7.035 mg substance: 7.19 ml N_2. Found %: C 48.36; H 5.52; N 14.32. $C_{12}H_{12}O_4N_2S$. Calculated %: C 48.48; H 5.15; N 14.14.

SUMMARY

A new compound $C_{12}H_{12}O_4N_2S$ was obtained by melting together sulfanilamide and bromoural, which the author regards as a 1,5-disubstituted derivative of hydantoin.

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ACONITE ALKALOIDS

V. ELDELINE AND ELDELIDINE

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The high toxicity of the various aconites of larkspur, a variety of plants rich in alkaloids, long ago attracted the attention of both Soviet and foreign investigators. During the past ten years there have been published about 10 Soviet and 20 foreign works, devoted to the study of this group of alkaloids, which is distinguished by marked physiological activity and extraordinary complexity of chemical structure.

Soviet investigators have already isolated upwards of twelve alkaloids from different varieties of larkspur and the aconites which grow in Soviet Union territory, and a relationship between them has been determined which enables all of the works on them to be incorporated into one group under the joint title of "The Aconite Alkaloids" [1]. The works of Konovalova and Orekhov [2] have also established a most interesting regularity, as follows: if one mentally substitutes all of the replaceable groups (hydroxyl, methoxyl, N-alkyl, and others) in the formulas of the aconite alkaloids by hydrogen, it will be seen that all lead to one and the same formula, $C_{19}H_{29}N$. In the following Soviet works – Rabinovich and Konovalova [3], Yunusov and Abubakirov [4], assumption was further made concerning the possibility of grouping the formulas of some of the aconite alkaloids under the general formula, $C_{20}H_{31}N$.

In Table 1 are listed alkaloids isolated by Soviet chemists over the past ten years.

The data quoted in the table unquestionably confirm Orekhov and Konovalova's assumption that the heterocyclic nucleus, $C_{19}H_{29}N$, or $C_{20}H_{31}N$, is common to all of the aconite alkaloids.

In the present article are reported the results of investigations of one variety of larkspur - Candle larkspur (Delphinium elatum). The variety indicated has been repeatedly investigated by various foreign workers. In the first work, published by Keller in 1925, there was reported the derivation of alkaloids from the seeds of this plant, in amounts approximating 1% of the seed weight, and the isolation of a crystalline alkaloid with a m.p. of 218°, of composition $C_{33}H_{51}O_8N$. In addition, Goodson [9] published an article in 1943, wherein he reported alkaloids from the seed of the same plant to the sum of 1.7%, from which the author isolated three crystalline alkaloids: delpheline, m.p. 227°, of the composition $C_{22}H_{39}O_5N$, delatine, m.p. 148°, of the composition $C_{19}H_{35}O_3N$, and methyllycaconitine in the form of the hydriodide, m.p. 201°, of the composition $C_{37}H_{48}O_{10}N_2 \cdot HI \cdot 2H_2O$. In 1944 the same author published a work [10] in which a different composition was ascribed to delpheline, namely $C_{25}H_{39}O_6N$.

Upon investigation of the variety of larkspur in question, the author has obtained results which differ from those published previously. Such a difference should be explained first of all by the fact that the authors mentioned studied the alkaloids obtained from the seeds, whereas this author studied the stems and the leaves. Secondly, geographical and climatic conditions are entirely different in the locality where the investigated specimens grow.

The candle larkspur specimen investigated by the author was collected by an expedition from the All Union Chemico-Pharmaceutical Institute of Scientific Research, under the direction of P. S. Massagetov during the period of the end of July and beginning of August, at blossoming time, along the banks of the river Ulba (in the Altai region).

All of that part of the plant which grows above ground was extracted with alcohol. The sum of the alkaloids isolated amounted to 0.25% of the plant dry weight. It should be noted that the alkaloid content of the leaves is considerably higher than that of the stems: thus, when the sum of the alkaloids in the leaves attains 0.85%, the stalks contain only 0.15% of the dry weight of initial raw material. Upon concentration of the ether extract, there immediately crystallized out an alkaloid, which, after purification in the form of its salt, melted at 182-184°, and exhibited a specific rotation of 32.46°. The alkaloid forms readily-crystallizable salts: hydrochloride, hydriodide, perchlorate, oxalate, nitrate. On the basis of an elementary analysis, both of the base and of its salts, it was possible to determine its composition $C_{27}H_{41}O_8N$.

TABLE 1

No.	Alkaloid	Composition	Partly-developed formula	Basic nucleus	Author
1	Thalatisamine	$C_{22}H_{35}O_4N$	$C_{19}H_{24}(NH)(OH)(OCH_3)_3$	$C_{19}H_{29}N$	Konovalova, Orekhov [2]
2	Thalatisidine	$C_{23}H_{37}O_5N$	$C_{19}H_{23}(NC_2H_5)(OH)_3(OCH_3)_2$	$C_{19}H_{29}N$	
3	Isothalatisidine	$C_{23}H_{37}O_5N$	$C_{19}H_{23}(NC_2H_5)(OH)_3(OCH_3)_2$	$C_{19}H_{29}N$	
4	Thalatisine	$C_{20}H_{29}O_3N$	$C_{19}H_{23}(NCH_3)(OH)_3$	$C_{19}H_{29}N$	
5	Delphamine	$C_{25}H_{41}O_7N$	$C_{20}H_{25}(NC_2H_5)(OH)_4(OCH_3)_2$	$C_{20}H_{31}N$	Konovalova and Rabinovich [3]
6	Condelphine	$C_{25}H_{39}O_6N$	$C_{19}H_{23}(NC_2H_5)(OH)_2(OCOCH_2)(OCH_3)_2$	$C_{19}H_{29}N$	The same [1]
7	Songorine	$C_{21}H_{29}O_3N$	$C_{18}H_{22}(NC_2H_5)(OH)_2(CO)$	$C_{19}H_{29}N$	Yunusov [5]
8	Delphatine	$C_{26}H_{43}O_7N$	$C_{19}H_{21}(NC_2H_5)(OH)_2(OCH_3)_5$	$C_{19}H_{29}N$	Abubakirov [6]
9	Delbine	$C_{38}H_{55}O_{10}N_3$	$C_{19}H_{21}(NC_2H_5)(OH)(OCH_3)_5(OCOC_6H_4NHCOCH(CH_3)CH_2CONH_2)$	$C_{19}H_{29}N$	
10	Delsamine	$C_{37}H_{53}O_{10}N_3$	$C_{19}H_{21}(NC_2H_5)(OH)_2(OCH_3)_4(OCOC_6H_4NHCOCH(CH_3)CH_2CONH_2)$	$C_{19}H_{29}N$	
11	Delsine	$C_{25}H_{41}O_7N$	$C_{19}H_{21}(NC_2H_5)(OH)_3(OCH_3)_4$	$C_{19}H_{29}N$	
12	Amino alcohol of delartine	$C_{26}H_{43}O_7N$	$C_{20}H_{25}(NC_2H_5)(OH)_3(OCH_3)_4$	$C_{20}H_{31}N$	Rabinovich and Konovalova [7]

The alkaloid isolated by the author contains three methoxyl, one hydroxyl and an N-alkyl group. The methoxyl and the N-alkyl groups were determined by the method of Fibock. The presence of the hydroxyl group was demonstrated by the formation of a monoacetyl derivative. It is of interest to note that the authors succeeded in acetylating the base only upon prolonged heating of the alkaloid with acetyl chloride in a sealed tube, similar to that of isothalatisidine [4], delphamine [5] and the amino-alcohol of delartin [6]. A new substance, of the composition $C_{29}H_{43}O_9N$, was obtained as the result. Upon heating with acetic anhydride in pyridine medium the unchanged base was recovered. Our alkaloid exhibits unusual behavior relative to methyl iodide, resembling in this respect the amino alcohol of delartine [6] and delsine [7]. As with the cases indicated, during this reaction the hydriodide of the initial alkaloid is formed, rather than the expected methyl iodide, exactly identical with the product which results when the alkaloid and hydriodic acid are interacted.

It should be observed that among the aconite bases described in the literature, is the known alkaloid, deltaline [11], isolated in 1936 from Delphinium occidentale. Deltaline, in its melting point, specific rotation and elementary analysis data, resembles very much the alkaloid isolated by the author from Candle larkspur. However, its resemblance is limited to these constants only; thus, according to the literature data, attempts to isolate any crystalline salts of deltaline were unsuccessful, whereas a pure alkaloid will form well-defined salts with both inorganic and organic acids. There was described only an auric salt of deltaline, which melted at 120-125°, whereas the chloraurate of our alkaloid melts at 175°. In agreement with the analytical data, deltaline was said to contain two methoxyl groups, and respectively was described its triacetyl derivative with m.p. 270-272°. The alkaloid isolated by the author contains three methoxyl groups and one hydroxyl group. The monoacetyl derivative obtained melts at 142-144°. Comparative data are quoted in Table 2.

Thus, the author has reason to believe that this is a new alkaloid which has not been described in the literature. The alkaloid has been named "eldeline" by the author.

Considerable difficulty was encountered in separating the alkaloid mixture obtained from the mother liquor after separation of eldeline. Attempts to apply the method of fractional separation based upon basicity, to obtain crystalline salts, and to utilize the methods of chromatography were all unsuccessful. The author finally

TABLE 2

Constants	Deltaline [11]	Base from Candle larkspur
Melting point and $[\alpha]_D$	180-181°; −27.86°	182-184°; −32.4°
Carbon content (%)	63.37, 63.71	64.10, 63.82
Methoxyl group content (%)	15.68	18.27
Functional group	$(OCH_3)_3(OH)_3$	$(OCH_3)_3OH$
Melting point of chloraurate	120-125°	170-175°
Melting point of acetyl derivative	270-272°	142-144°

succeeded in isolating another crystalline alkaloid only by discovering an interesting property – the solubility of its sulfate in chloroform. Base No. 2, thus isolated, is much more difficultly soluble in organic solvents than is eldeline. After recrystallization from alcohol, the alkaloid, not yet carefully studied, melted at 212-214°. After removal of eldeline and base No. 2, there still remains about 0.1% of a non-crystallizable mixture of alkaloids, procedures for the separation of which are still under investigation.

Eldeline was found to be an ester, which saponified upon heating the base in a water-alcohol solution of alkali. Accordingly, a crystalline amino alcohol was isolated, crystallizing well from alcohol, with a m.p. of 226-228°, and with a specific rotation of −17.08°. The amino alcohol obtained by the author forms well-defined salts: hydrochloride, hydriodide, nitrate and oxalate. According to the elementary analysis data, both of the base and of its salts, the composition of the amino alcohol was determined to be $C_{25}H_{39}O_7N$. As can be seen from the empirical formula of eldeline $C_{27}H_{41}O_8N$, and its amino alcohol $C_{25}H_{39}O_7N$, the first is found to be the acetate ester of the second.

Determination of functional groups in the amino alcohol has demonstrated the presence of three methoxyl, two hydroxyl and one N-alkyl group. The nature of the two remaining oxygen atoms was clarified by determination of the presence, in the amino alcohol, of the methylenedihydroxy group, proven by the known qualitative reaction obtained upon heating with phloroglucinol. The character of the N-alkyl group was ascertained by oxidation of the amino alcohol. Upon reaction of an acid solution of potassium permanganate, followed by cooling, there occurred a splitting off of the N-alkyl group to form an aldehyde, as was proven to be the case with delphamine [3], condelphine [1] and other alkaloids of the aconite group. With an N-methyl group there is formed formaldehyde; in the presence of an N-ethyl group there is formed acetaldehyde. Upon oxidation of the amino alcohol of eldeline, formaldehyde separated, which was identified by its condensation product with dimedone.

In this manner, the partially-developed formulas for eldeline and for its amino-alcohol are found to be as follows:

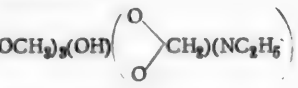
Eldeline $C_{27}H_{41}O_8N$ $C_{20}H_{23}$ $\langle (OCH_3)_3, (OH), (OCOCH_3), \begin{pmatrix} O \\ \diagdown\ \diagup\ CH_2 \\ O \end{pmatrix}, (NCH_3) \rangle$

Amino alcohol of eldeline $C_{25}H_{39}O_7N$ $C_{20}H_{23}$ $\langle (OCH_3)_3, (OH)_2, \begin{pmatrix} O \\ \diagdown\ \diagup\ CH_2 \\ O \end{pmatrix}, (NCH_3) \rangle$

and of course the framework of these two new aconite alkaloids is their characteristic heterocyclic ring.

The amino alcohol behaves like eldeline in its reaction with methyl iodide; instead of the expected methyl iodide (addition complex), the hydriodide of the original base is formed. A study of the acetylation of the amino alcohol yielded interesting results: there was formed the monoacetyl derivative of the alcohol, found to be identical with eldeline, when the former was reacted with acetic anhydride in pyridine. Reaction with acetyl chloride yielded the diacetyl derivative, found to be identical with the monoacetyl derivative of eldeline. Saponification of the latter with a water-alcohol solution of alkali yielded the unchanged amino alcohol. In

TABLE 3

	Delpheline [9,10]	Amino alcohol of eldeline
Base	M.p. 227° $[\alpha]_D = -25.8°$	M.p. 226-228° $[\alpha]_D = -17.08°$
Hydrochloride	M.p. 219° $[\alpha]_D = -42.8°$	M.p. 214-216° $[\alpha]_D = -31.3°$
Nitrate	M.p. 191-193° $[\alpha]_D = -41.2°$	M.p. 186-188° $[\alpha]_D = -41.4°$
Base content	$C_{25}H_{39}O_6N$ [10]	$C_{25}H_{39}O_7N$
Functional groups	$(OCH_3)_3(OH)$ 	$(OCH_3)_3(OH)_2$
Monoacetyl derivative	M.p. 125° $[\alpha]_D = -34.5°$	182-184° $[\alpha]_D = -32.46°$
Diacetyl derivative	–	M.p. 142-144° $[\alpha]_D = -25.4°$

this way, by saponification and by acetylation, the author has succeeded in proving that eldeline is the acetate ester of the amino alcohol.

The author has shown above that the bases isolated from the given specimen of Delphinium elatum differ from the alkaloids described in the literature; however, the product of saponification obtained by the author – the amino alcohol of eldeline – resembles in its properties the alkaloid delphine, isolated by Goodson [9] in 1943 from the plant species named. The isolation of two bases from one and the same plant species makes their identity quite possible. However, a more thorough investigation of the amino-alcohol of eldeline proved that these substances are different. In Table 3 the properties of the two bases are compared.

As can be seen from the data quoted, these bases differ in their composition, in the number of hydroxyl groups, the character of the N-alkyl group, and in the properties of the acetyl derivatives. Thus, the amino alcohol of eldeline is found to be a new substance, not described in the literature, which gives the author the privilege of naming it "eldelidine".

All of the analytical determinations were conducted in the microanalysis laboratory under the supervision of candidate of chemical science V. V. Kolpakova. The author is very much indebted to her for these determinations.

EXPERIMENTAL

1. Isolation and Separation of the Alkaloids. 10 g of the pulverized plant was extracted with isopropyl alcohol, containing 1% of acetic acid. The alcohol extract was steamed in vacuo at a water bath temperature not exceeding 40-50°. The thick resinous substance obtained was dissolved in 10% sulfuric acid, and the acid solution was treated with benzene to remove the resin. The considerably clarified sulfate solution, after cooling with ice, was made alkaline with 25% ammonia, after which exhaustive extraction with diethyl ether was made. After the ether extract had been dried with anhydrous sodium sulfate, the ether was distilled off to a volume of 100-120 ml. After cooling the concentrated solution, a base crystallized out, named "eldeline", in the form of light-colored needle crystals, which were vacuum filtered, washed with diethyl ether and dried in a vacuum dessicator. 11 g of crude eldeline was isolated, m.p. 176-180°. The mother liquor, after separation of the eldeline, was treated with 10% sulfuric acid. The sulfate solution so obtained was extracted with approximately five times the volume of chloroform.

a) Treatment of the chloroform solution. The chloroform was distilled off in vacuo, and the remaining syrupy substance was dissolved in a few ml of 10% sulfuric acid, and the acid solution was washed several times with ether, and then made alkaline with 25% ammonia, and then exhaustively extracted with ether. After steaming off the latter, there crystallized out about 1 g of Base No. 2, with a m.p. of 204-208°. After recrystallization from 10 times its volume of 96% alcohol, the base melted at 212-214°.

b) Treatment of the sulfate solution. The acid aqueous solution remaining after the chloroform extraction was made alkaline with 25% ammonia and then exhaustively extracted with ether. After concentration of the ether solution, an additional 2 g of eldeline crystallized out, and there remained about 10-11 g of a non-crystallizing alkaloid mixture, which has not as yet been investigated.

In all, there were isolated, from 10 kilograms of raw material, 13 g of eldeline, 1 g of Base No. 2 and 10-11 g of non-crystallizable bases. The sum total of the alkaloids thus consisted of 25 g, or 0.25% of the dry weight of the above-ground portions of the plant.

Upon separation of the alkaloids by the described method, there were obtained, separately, from the leaves and from the stems, the following results. From 1 kg of leaves there were isolated 4 g of eldeline and 4.3 g of non-crystallizable bases. The total sum of alkaloids was 8.3 g, or 0.83% of the dry weight of leaves. From 1 kg of stems there was isolated 0.5 g of eldeline and 1 g of non-crystallizable bases. The total sum of alkaloids was 1.5 g or 0.15% of the dry weight of stems.

2. Eldeline. The technical base, m.p. 176-180°, was purified by subsequent transformation into the hydrochloride and into the oxalate. The base, isolated from an aqueous solution of salt by the action of ammonia, was extracted with ether and recrystallized by concentration of the latter. After recrystallization from diethyl ether (1:50), it melted at 182-184°. Eldeline is difficult to dissolve in water, petroleum ether and diethyl ether; more soluble in ethyl acetate, and readily soluble in acetone, alcohol and chloroform.

0.1642 g substance: 3.25 ml alcohol; $l = 0.5$; $\alpha = -0.82°$; $[\alpha]_D = -32.46°$. 3.271 mg substance: 7.688 mg CO_2; 2.374 mg H_2O. 4.320 mg substance: 10.109 mg CO_2; 3.112 mg H_2O. 8.395 mg substance: 0.235 ml N_2 (22.0°, 728 mm). 7.145 mg substance: 0.183 ml N_2 (27.5°, 727 mm). 8.910 mg substance: 0.60 ml CH_4 (18°, 740 mm). 8.584 mg substance: 0.60 ml CH_4 (25°, 750 mm). 5.433 mg substance: 9.60 ml 0.02 N $Na_2S_2O_3$. 0.0932 g substance: 1.85 ml 0.1 N HCl (methyl red). Found %: C 64.10, 63.82; H 8.12, 8.06; N 3.10, 2.78; (OCH_3) 18.27; M 503.8. $C_{27}H_{41}O_8N$. Calculated %: C 63.91; H 8.08; N 2.76; 3(OCH_3) 18.34; M 507.

3. Eldeline Salts. Hydrochloride. Eldeline was mixed with an equal volume of absolute alcohol, and upon addition of alcoholic hydrochloric acid, up to the point of a slightly acid reaction to Congo red, it all went into solution. Upon gradual addition of five times the volume of absolute ether, the hydrochloride crystallized out. After recrystallization from 10 times the volume of an acetone-absolute alcohol mixture (10:1), the hydrochloride melted at 204-206° (with decomposition).

0.1120 g substance: 3 ml water; $l = 0.5$; $\alpha = -0.95°$; $[\alpha]_D = -50.89°$.

5.000 mg substance: 1.415 mg AgCl. 5.494 mg substance: 1.554 mg AgCl. Found %: Cl 7.00, 7.00. $C_{27}H_{41}O_8N \cdot HCl$. Calculated %: Cl 6.53.

Nitrate. It was obtained by mixing an acetone solution of eldeline with nitric acid, and precipitating it from the obtained solution by the use of absolute ether. It was recrystallized from absolute alcohol (1:10), crystallizing out upon addition of absolute ether; m.p. 170-173° (with decomposition).

0.0750 g substance: 3 ml water; $l = 0.5$; $\alpha = -0.6°$; $[\alpha]_D = -48°$.

5.478 mg substance: 11.450 mg CO_2; 3.649 mg H_2O. 3.314 mg substance: 6.927 mg CO_2; 2.147 mg H_2O. 7.180 mg substance: 0.331 ml N_2 (21°, 732.5 mm). 8.00 mg substance: 0.372 ml N_2 (21.5°, 732 mm). Found %: C 57.00, 57.00; H 7.45, 7.24; N 5.16, 5.20. $C_{27}H_{41}O_8N \cdot HNO_3$. Calculated %: C 56.84; H 7.36; N 4.91.

Perchlorate. It was obtained by adding a saturated aqueous solution of sodium perchlorate to a solution of eldeline in 5% hydrochloric acid. After recrystallization from absolute alcohol (1:20), it melted at 216-217° (with decomposition).

Hydriodide. It was obtained by mixing an acetone solution of the base with hydriodic acid, and it separated out upon addition of dry ether. It was recrystallized from acetone (1:30), from which it crystallized out upon addition of dry ether; m.p. 219-220° (with decomposition).

5.817 mg substance: 5.39 ml 0.01 N $Na_2S_2O_3$. 6.401 mg substance: 5.89 ml 0.01 N $Na_2S_2O_3$. Found %: I 19.60, 19.47. $C_{27}H_{41}O_8N \cdot HI$. Calculated %: I 20.0.

Oxalate. It was obtained by mixing equimolecular quantities of eldeline and of oxalic acid dissolved in acetone. It was recrystallized from 10 times the volume of acetone mixed with absolute alcohol (3:1), m.p. 190-191° (with decomposition).

0.0816 g substance: 3.1 ml alcohol; $l = 0.5$; $\alpha = -0.55$; $[\alpha]_D = -41.7°$. 3.531 mg substance: 7.519 mg CO_2; 2.252 mg H_2O. 7.486 mg substance: 12.47 ml 0.02 N $Na_2S_2O_3$. 4.941 mg substance: 7.44 ml

0.02 N $Na_2S_2O_3$. Found %: C 58.07; H 7.13; (OCH_3) 15.40, 15.56. $C_{27}H_{41}O_8N$. $C_2H_2O_4$. Calculated %: C 58.29; H 7.2; 3(OCH_3) 15.58.

Chloraurate. It was obtained by the addition of auric chloride to a solution of the base in 5% hydrochloric acid. It separated in the form of an amorphous flocculent precipitate, readily soluble in alcohol. Upon addition of a few drops of water to the alcoholic solution, the chloraurate separated in the form of a fine crystalline precipitate with m.p. 170-175°. It failed to recrystallize.

4. Methyl Iodide Reaction. 1 g of eldeline was dissolved in 3 ml of methyl alcohol, and after cooling 1 ml of methyl iodide was added. The solution was heated in a sealed tube at 70-75° for 3 hours. After cooling, the tube contents were evaporated to dryness, and the residue repeatedly treated with boiling ether to ensure complete removal of all traces of the initial eldeline. The residue, in the amount of 0.5 g, was recrystallized from 20 ml of acetone. Upon addition of dry ether, there crystallized from the filtrate the substance with a m.p. of 220-221° (with decomposition). The sample, when mixed with the hydriodide of eldeline, did not produce depression of the melting point. The base obtained by pouring into an aqueous solution of ammonia did not give a depression with eldeline.

5. Acetylation of Eldeline. 1) To 0.25 g of eldeline was added 2 ml of dry pyridine and 2 ml of acetic anhydride – within a few minutes everything was dissolved. The reaction mixture was heated at 50-60° for 15 hours, after which the pyridine and the excess acetic anhydride were driven off in vacuo. The residue was dissolved in 2-3 ml of 10% sulfuric acid, and upon cooling was acidified with 10% ammonia solution – the separated base was recrystallized from ether, and thereupon melted at 180-182°. The sample mixed with eldeline did not produce depression.

2) To 0.5 g of eldeline was added 15 ml of acetyl chloride – the resulting mixture was heated in a sealed tube at 35-40° for 35 hours, as the result of which everything dissolved. After removal of the excess acetyl chloride, the residue was dissolved in a few ml of water, and upon cooling, the solution was acidified with 10% ammonia. The isolated base was readily soluble in a majority of the organic solvents. It was possible to recrystallize it from only 5 times the volume of hexane, after which the base melted at 142-144°.

0.1208 g substance: 3 ml alcohol; $l = 0.5$; $\alpha = -0.51°$; $[\alpha]_D = -25.4°$.
6.158 mg substance: 11.915 mg CO_2; 3.429 mg H_2O. 3.740 mg substance: 8.645 mg CO_2; 2.556 mg H_2O. 8.510 mg substance: 0.204 ml N_2(24.5°, 730 mm). 8.430 mg substance: 0.206 ml N_2 (25°, 727 mm). 7.486 mg substance: 12.37 ml 0.02 N $Na_2S_2O_3$. 6.806 mg substance: 11.12 ml 0.02 N $Na_2S_2O_3$. Found %: C 63.00, 63.04; H 7.44, 7.65; N 2.64, 2.68; OCH_3 17.08, 16.88. $C_{29}H_{43}O_9N$. Calculated %: C 63.39; H 7.83; N 2.5; 3(OCH_3) 16.9.

6. Saponification of Eldeline. 5 g of eldeline was dissolved in 25 ml of alcohol, to the solution was added 20 ml of 1 normal NaOH solution, and the reaction mixture was heated on a water bath for 3 hours, after which it was evaporated almost to dryness. The semi-crystalline mass was washed with water and dried in a vacuum dessicator. The yield of base was 4.3 g, with a m.p. of 220-224°. It was recrystallized from 6 times the volume of alcohol – a colorless, crystalline substance which melted at 226-228° (with the formation of bubbles).

The aminoalcohol obtained, named "eldelidine", was almost insoluble in water, difficult to dissolve in ether, easier to dissolve in acetone and alcohol, and very easy to dissolve in chloroform.

0.2190 g substance: 3.4 ml chloroform; $l = 0.5$; $\alpha = -0.55°$; $[\alpha]_D = -17.08°$

5.318 mg substance: 12.582 mg CO_2; 4.021 mg H_2O. 3.534 mg substance: 8.344 mg CO_2; 2.678 mg H_2O. 8.645 mg substance: 0.249 ml N_2 (22.0°, 728 mm). 8.535 mg substance: 0.250 ml N_2 (24.5°, 734 mm). 6.106 mg substance: 11.78 ml 0.02 N $Na_2S_2O_3$. 0.2294 g substance: 5 ml 0.1 N HCl methyl red. Found %: C 64.52, 64.39; H 8.46, 8.47; N 3.19, 3.24; (OCH_3) 19.94; M 458.8. $C_{25}H_{39}O_7N$. Calculated %: C 64.52; H 8.38; N 3.01; 3(OCH_3) 20.0; M 465.0.

7. Eldelidine Salts. Hydrochloride. It was obtained by mixing an alcoholic solution of eldelidine with hydrochloric acid, and it crystallized out upon addition of absolute ether. It recrystallized from absolute alcohol (1:20) upon addition of an equal volume of absolute ether to an alcoholic filtrate. It melted at 216-218° (with decomposition).

0.1104 g substance: 3.6 ml water; $l = 0.5$; $\alpha = -0.48°$; $[\alpha]_D = -31.3°$.

4.910 mg substance: 1.477 ml AgCl. Found %: Cl 7.44. $C_{25}H_{39}O_7N \cdot HCl$. Calculated %: Cl 7.08.

Nitrate. It was obtained by mixing an acetone solution of eldelidine with nitric acid. It was recrystallized from aqueous acetone, after which it melted at 186-188° (with decomposition).

0.0374 g substance: 3.5 ml water; $l = 0.5$; $\alpha = -22°$; $[\alpha]_D = -41.4°$.

4.228 mg substance: 8.864 mg CO_2; 2.991 mg H_2O. 3.411 mg substance: 7.142 mg CO_2; 2.419 mg H_2O. 8.680 mg substance: 0.400 ml N_2 (22.0°, 738 mm). 7.768 mg substance: 0.359 ml N_2 (22.0°, 738 mm). Found %: C 57.17, 57.10; H 7.92, 7.94; N 5.18, 5.19. $C_{25}H_{39}O_7N \cdot HNO_3$. Calculated %: C 57.1; H 7.6; N 5.33.

Oxalate. It was obtained by mixing acetone solutions of equimolecular weights of the eldelidine and the oxalic acid. The oxalate recrystallized from 20 times the volume of acetone-absolute alcohol mixture (5:1), after which it melted at 140-142° (with decomposition).

3.203 mg substance: 6.688 mg CO_2; 2.103 mg H_2O. 2.037 mg substance: 4.221 mg CO_2; 1.361 mg H_2O. Found %: C 56.47, 56.51; H 7.35; 7.47. $C_{25}H_{39}O_7N \cdot C_2H_2O_4 \cdot H_2O$. Calculated %: C 56.54; H 7.50.

Hydriodide. It was obtained by neutralization with hydriodic acid of an acetone solution of the eldelidine, and was separated from solution by the addition of dry ether. It recrystallized from a mixture of acetone-alcohol, after which it melted at 217-219° (with decomposition).

0.0654 g substance: 2.7 ml water; $l = 0.5$; $\alpha = -0.3°$; $[\alpha]_D = -24.7°$.

8. Methyl Iodide Reaction. 0.5 g of eldelidine was dissolved in 5 ml of methyl alcohol and 1 ml of methyl iodide was then added and the solution obtained was heated in a sealed tube at 70-75° for 6 hours. After cooling, the tube contents were poured into a beaker and the excess methyl alcohol and methyl iodide driven off. The remaining crystalline substance was treated with water. An insoluble substance, to the amount of 0.2 g, was found to be present in the original eldelidine. From the aqueous solution, upon addition of ammonia, the unchanged eldelidine was recovered.

9. Acetylation of Eldelidine. 1) 0.3 g of eldelidine was mixed with freshly distilled acetic anhydride and 2.5 ml of dry pyridine. The solution obtained was heated on a water bath at 35-40° for 8 hours, after which the acetic anhydride and pyridine excesses were distilled off in vacuo. The syrupy residue was dissolved in a few milliliters of 5% sulfuric acid, the acid solution washed with ether, and then made basic with 25% ammonia solution. The base, which immediately separated, melted at 180-182°, and the sample mixed with eldelidine did not produce depression.

2) 0.5 g of eldelidine was combined with 5 ml of acetyl chloride and heated in a sealed tube at 40-50° for 40 hours, after which everything went into solution. After cooling the solution, the acetyl chloride excess was evaporated off at room temperature and the residue dissolved in 5 ml of water. The aqueous solution (after cooling in ice) was made basic with 10% ammonia solution, in the presence of ether. The separated base immediately went into the ether (layer). After concentrating the ether extract to a small volume, 0.4 g of the substance crystallized. After recrystallization from 50% alcohol (1:4), the base melted at 142-144°. A sample mixed with acetyleldeline did not give depression of the melting point.

Hydrochloride. It was obtained by neutralization of an ether solution of acetyleldeline with an alcoholic solution of hydrochloric acid. After recrystallization from 10 times the volume of an absolute ether-acetone mixture (1:2), the hydrochloride melted at 172-174°.

5.195 mg substance: 1.360 mg AgCl. 3.919 mg substance: 1.103 mg AgCl. Found %: Cl 6.47, 6.33. $C_{29}H_{43}O_9N \cdot HCl$. Calculated %: Cl 6.06.

10. Saponification of Acetyleldeline. 0.5 g of acetyleldeline was dissolved in 5 ml of alcohol, after which was added 5 ml of 1 N NaOH solution, followed by heating for three hours on a water bath, after which the solution was evaporated. The residue was treated with water, vacuum filtered, washed with aqueous alcohol, and melted at 226-228°. A sample mixed with eldelidine did not produce depression.

11. Oxidation of Eldelidine. 1 g of eldelidine was dissolved in 10 ml of 10% sulfuric acid solution. 0.34 g of potassium permanganate in 10 ml of water was added from a dropping funnel over a period of 1 hour, with stirring and cooling, to the obtained solution. After another hour of mixing, the solution lost its color, the manganese dioxide was filtered off and the filtrate was distilled into a receiver well-cooled with ice. 50 ml of 1% warm aqueous dimedone solution was added to the distillate obtained, and within a few seconds the solution became turbid, after heating for 15-20 minutes of which, the bulky flocculent precipitate, first formed, then

changed into a crystalline substance. 0.12 g of the condensation product was vacuum filtered, and recrystallized from 4 ml of hexane, after which it melted at 183-184°. The condensation product of dimedone with formaldehyde melts at 185-186°. The mixed sample did not produce depression; it melted at 184-185°.

12. Determination of the dihydroxymethylene grouping. 0.02 g of eldelidine was dissolved, with heating, in 5 ml of phloroglucinol-sulfuric acid mixture. After heating on a boiling water bath, a flocculent precipitate appeared, and the solution became red, characteristic for substances with the dihydroxymethylene group.

SUMMARY

1. There has been isolated a new crystalline alkaloid of the composition $C_{27}H_{43}O_8N$ from Candle larkspur (Delphinium elatum), which grows in the Altai region, which has been named "eldeline".

2. Eldeline has been found to be an ester, and upon its saponification there is formed acetic acid and a crystalline amino alcohol of the composition $C_{25}H_{41}O_7N$, named "eldelidine".

3. The partly-developed formulas of eldeline and of eldelidine have been determined:

eldeline $C_{27}H_{41}O_8N = C_{20}H_{23}(OCH_3)_5(OH)\left(\begin{matrix}O\\ \diagup\ \diagdown\\ O\end{matrix}CH_2\right)(OCOCH_3)(NCH_3)$;

eldelidine $C_{25}H_{39}O_7N = C_{20}H_{23}(OCH_3)_5(OH)_2\left(\begin{matrix}O\\ \diagup\ \diagdown\\ O\end{matrix}CH_2\right)(NCH_3)$.

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